FIGURE 1

AFP E1a and E1b Adenovirus Constructs

FIGURE 2A

Huh-7 Cells (AFP+)

Dld-1 Cells (AFP-)
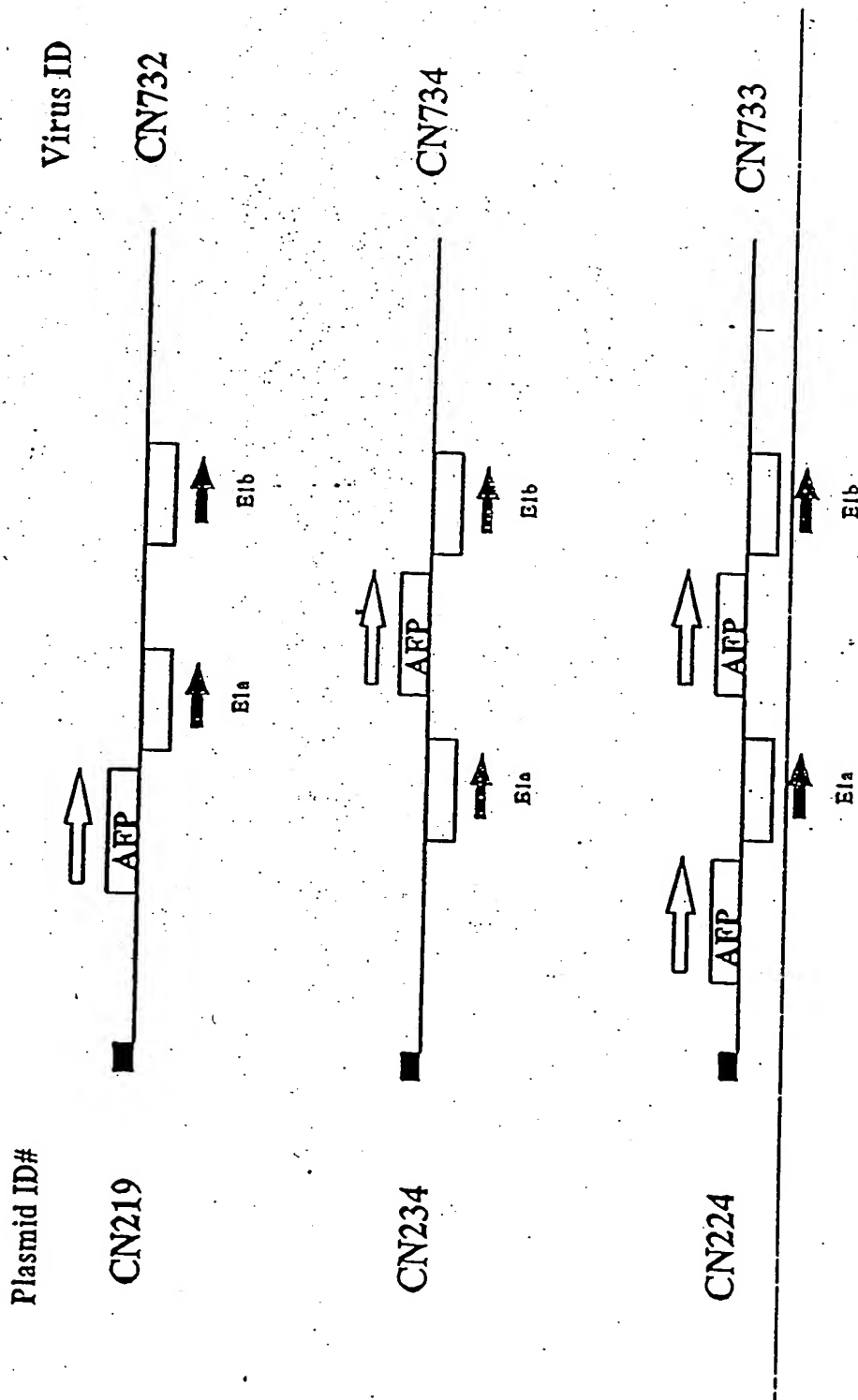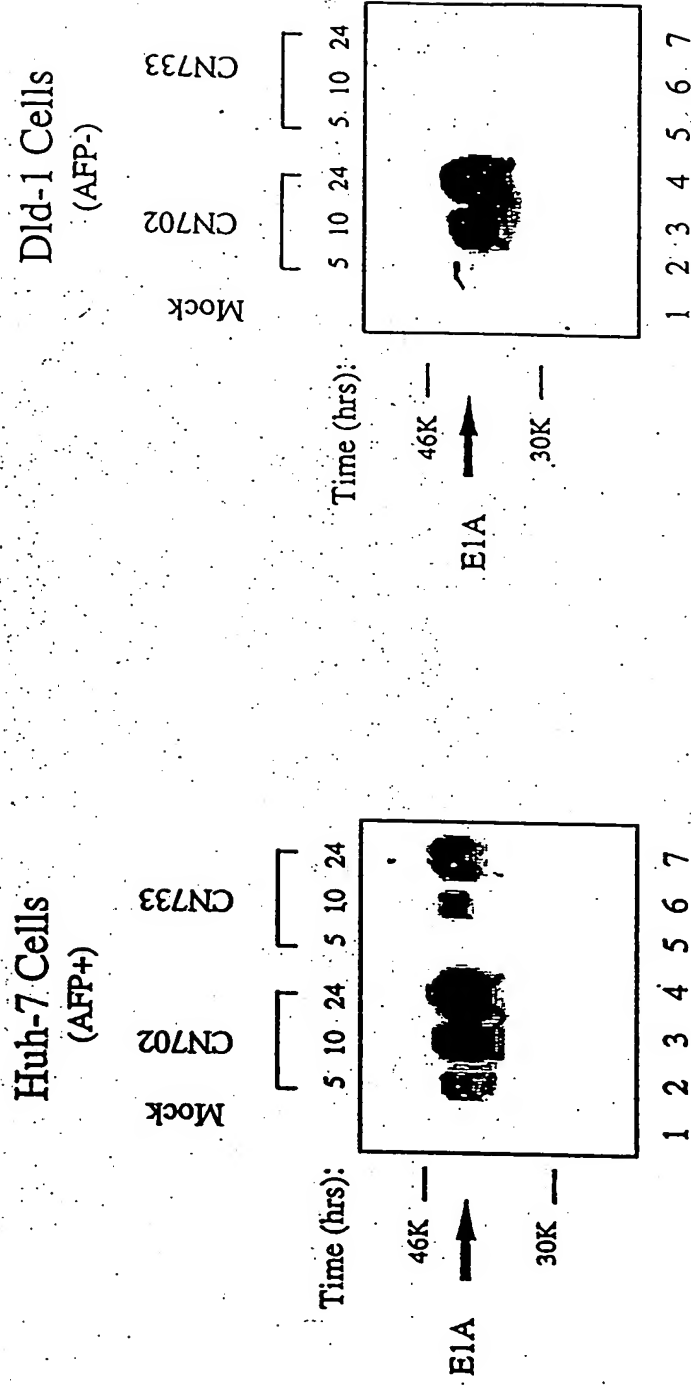
FIGURE 2B

FIGURE 3A

Huh-7
(AFP+)
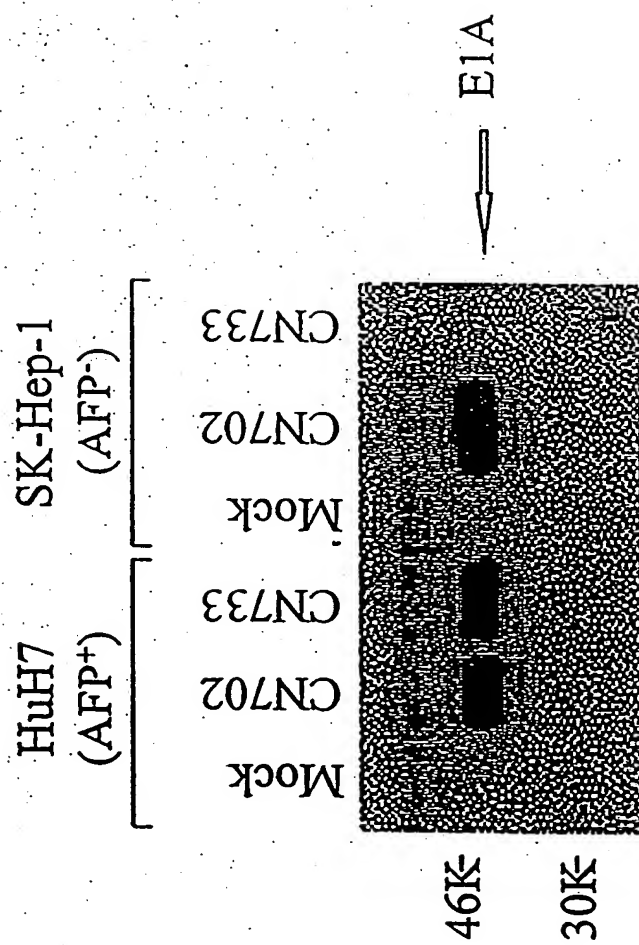
FIGURE 3B

Sk-Hep-1
(AFP-)

FIGURE 3C

Dld-1
(AFP-)

Virus Yield (PFU)

10000000
1000000
100000
10000
1000
100
10

0   20   40   60   80   100

Time (hrs)

CN702
CN733
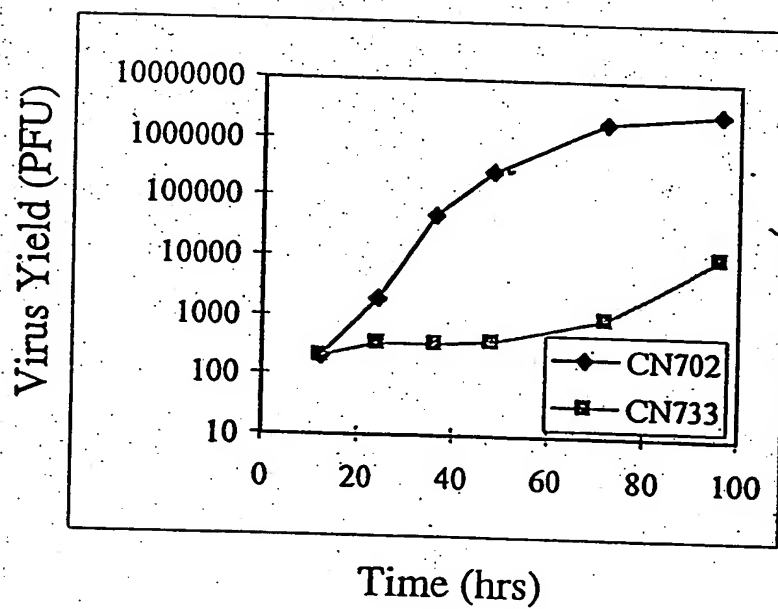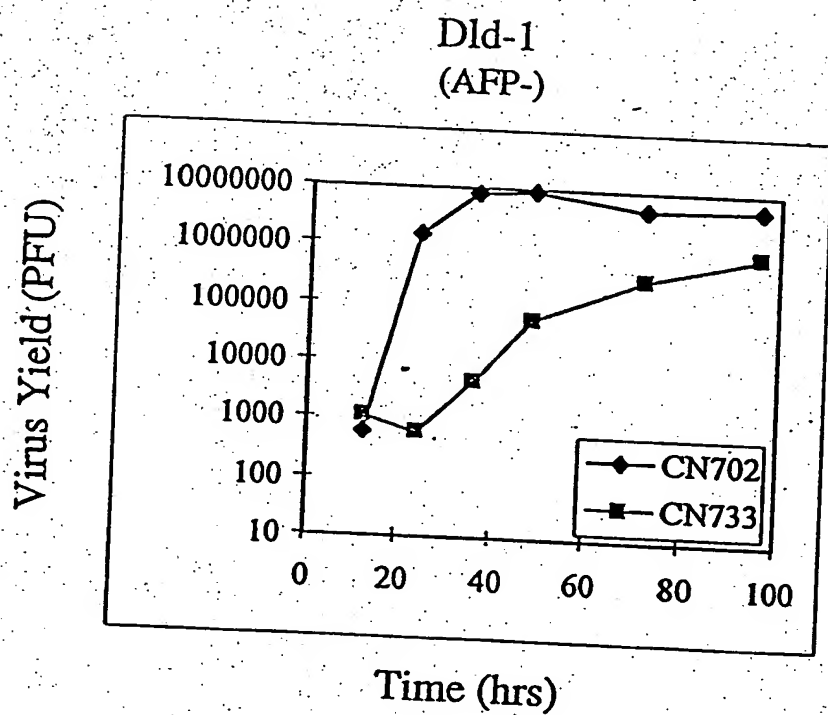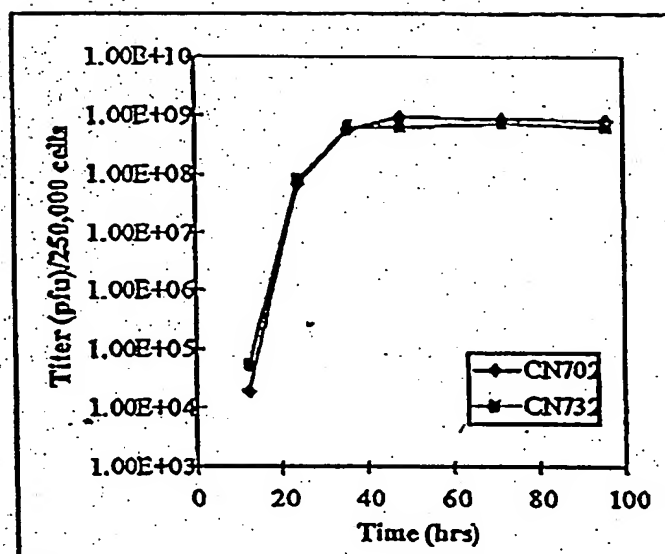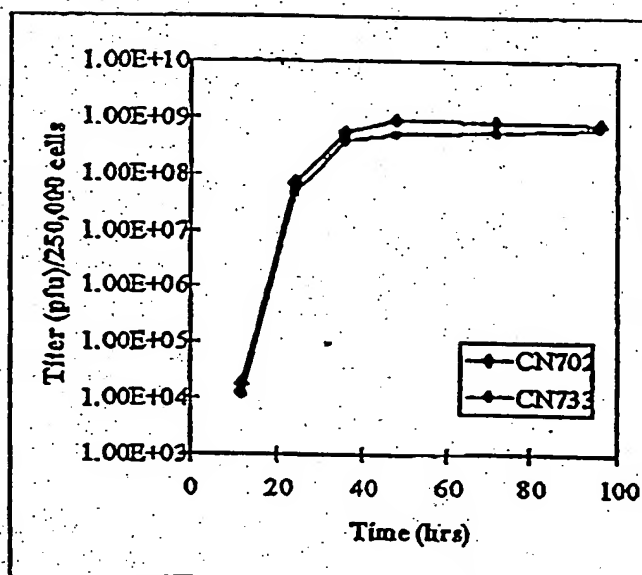
FIGURE 4A

FIGURE 4B

FIGURE 4C
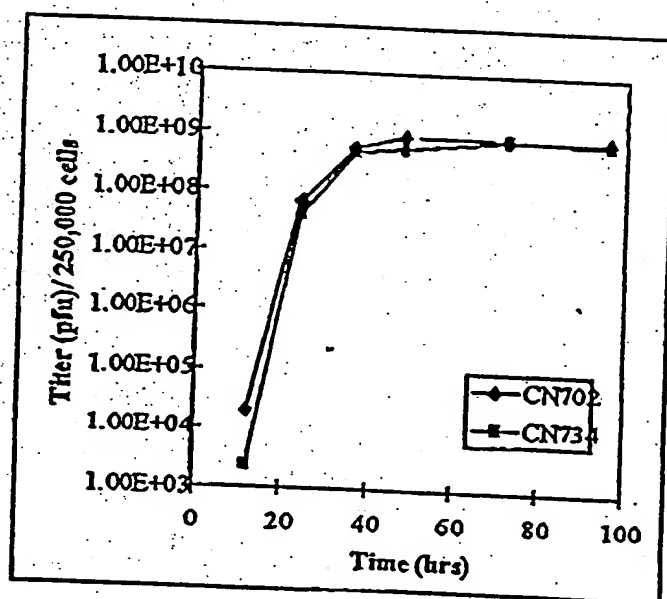
FIGURE 5A
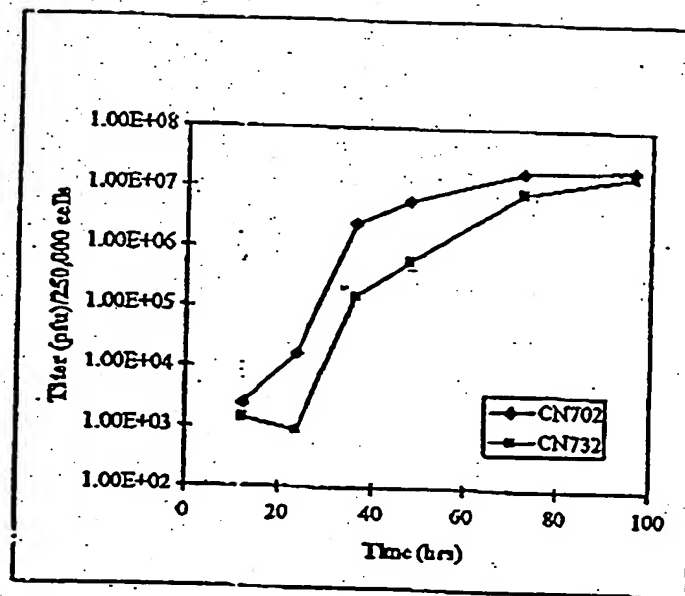
FIGURE 5B
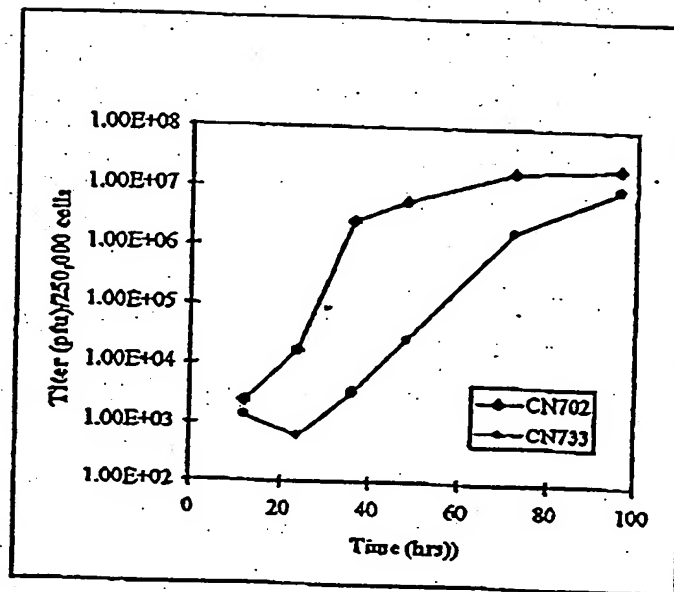
FIGURE 6A
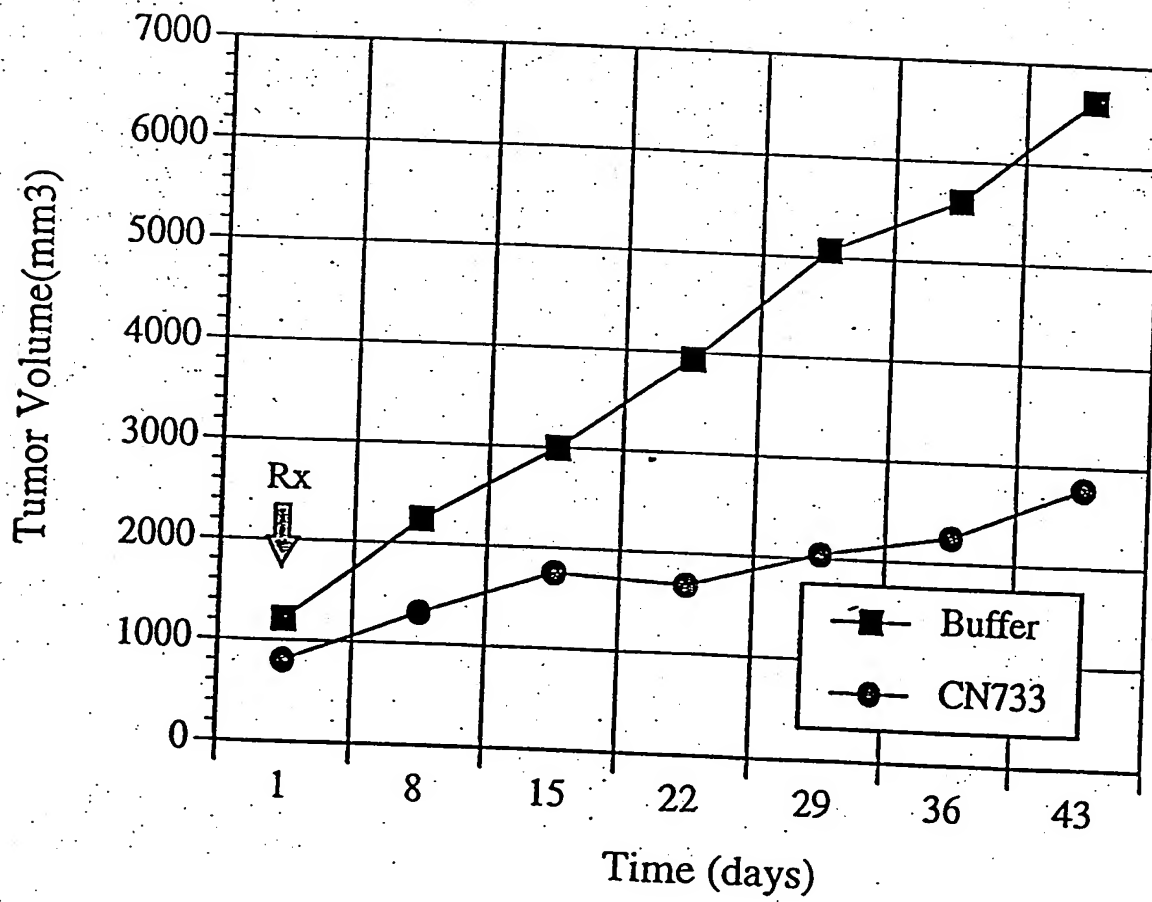
FIGURE 6B
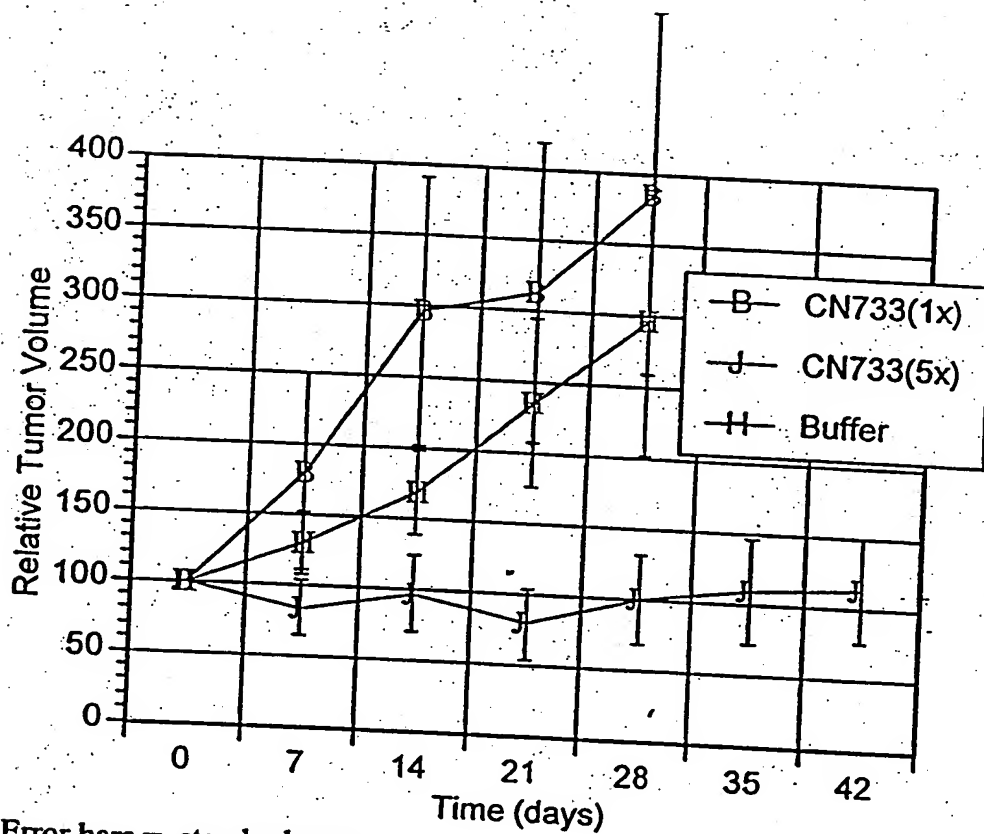
Error bars = standard error
Animals from groups treated with a single dose of CN733 and buffer were sacrificed at 28 days because of excessive tumor burden

FIGURE 7

Y-axis: [Serum AFP] x 10⁴ (ng/ml) — labeled 0, 20, 40, 60, 80, 100, 120, 140, 160, 180

X-axis: Time (weeks) — labeled 0, 1, 2, 3, 4, 5, 6

Legend:
—o— Buffer
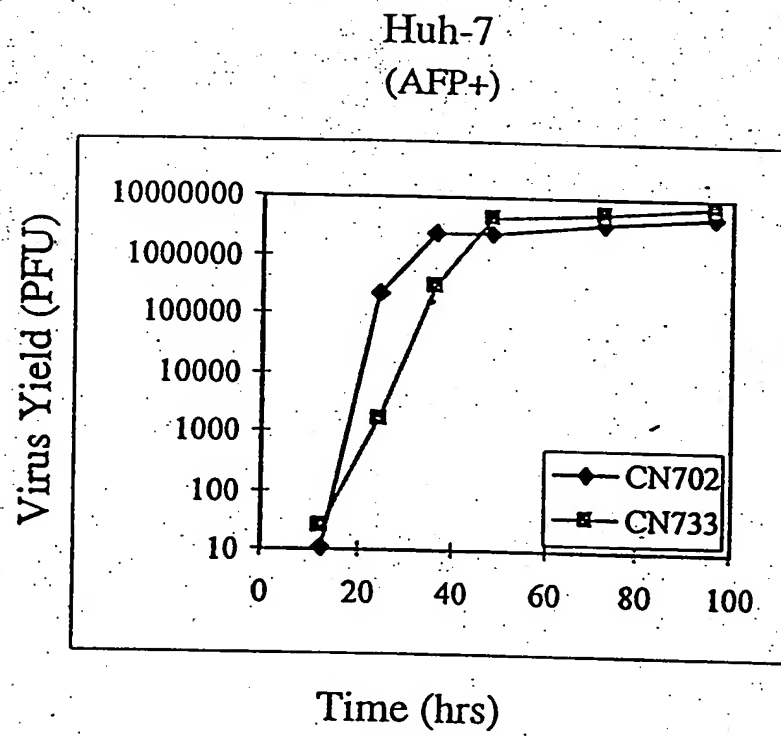—△— CN733
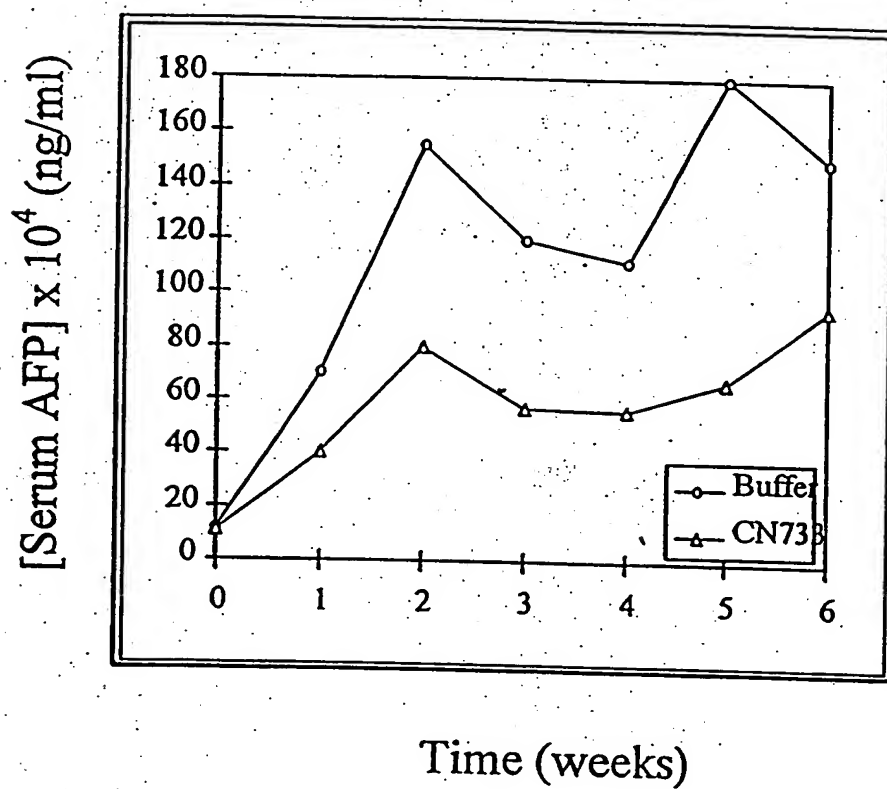
FIGURE 8

CEA E1a and E1b Adenovirus Constructs
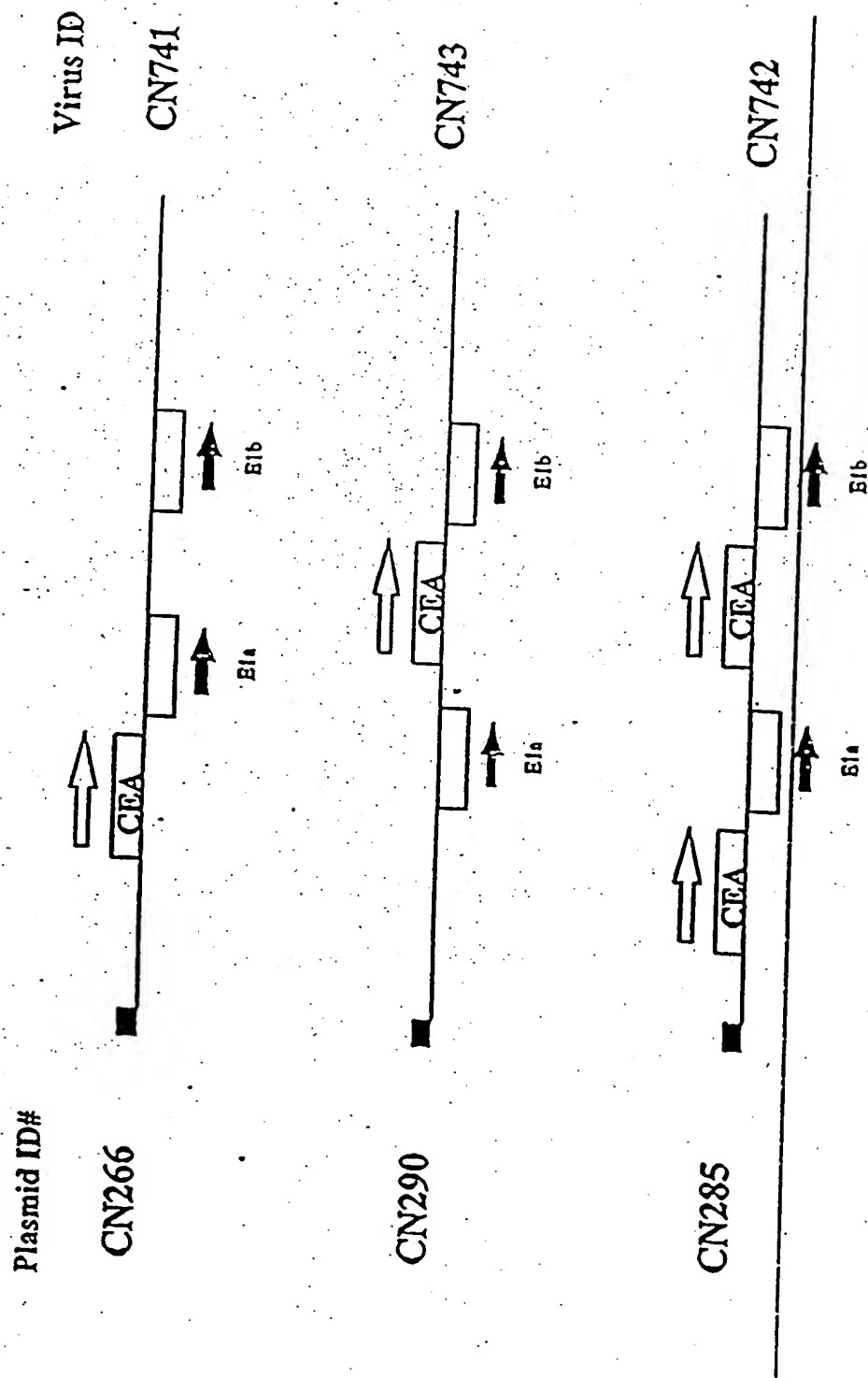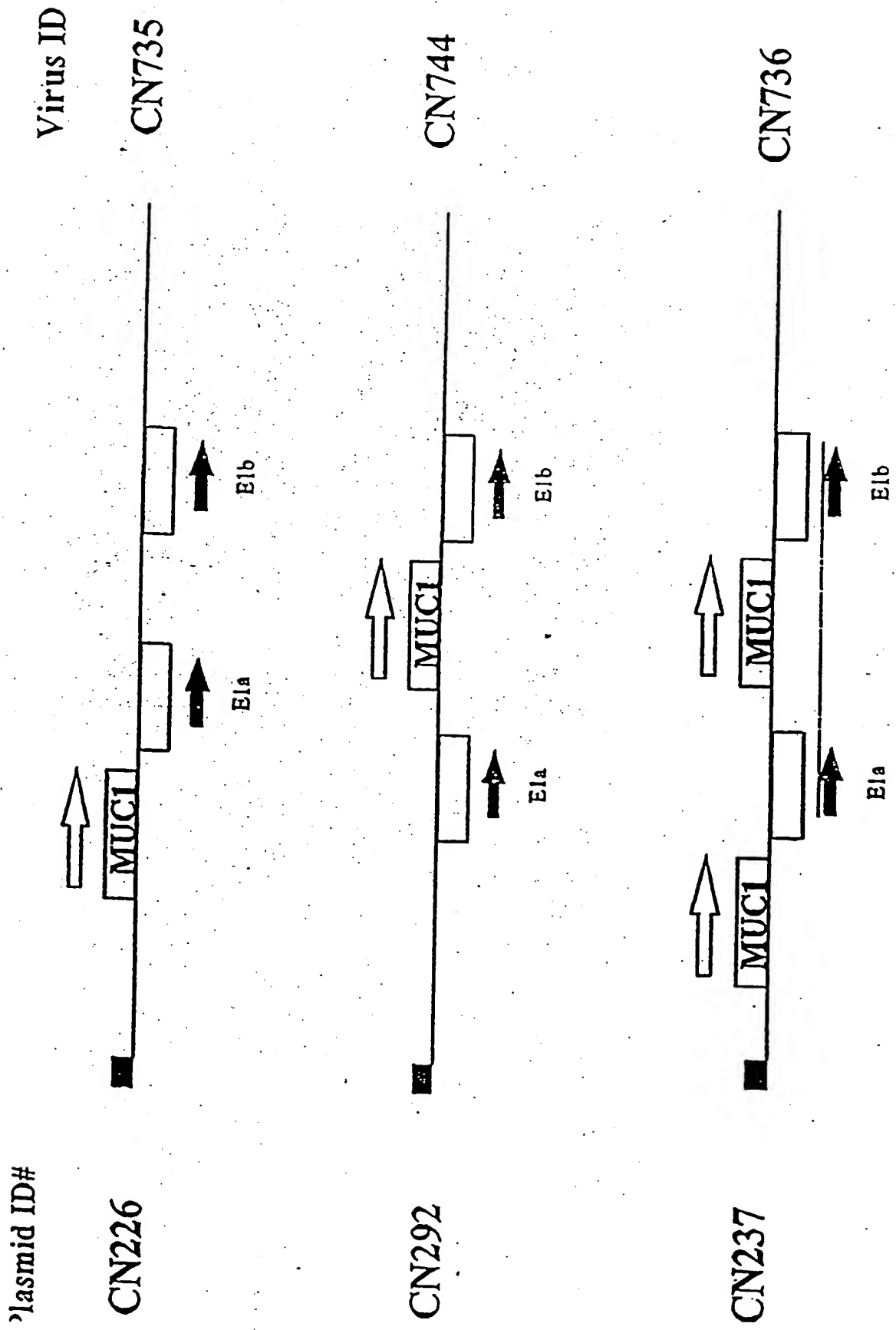
FIGURE 9

-426

5'-AAGCTTCCACAAGTGCATTTAGCCTCTCCAGTATTGCTGATGAATCCACAGT

TCAGGTTCAATGGCGTTCAAAACTTGATCAAAAATGACCAGACTTTATATTCTTA

CACCAACATCTATCTGATTGGAGGAATGGATAATAGTCATCATGTTTAAACATCT

ACCATTCCAGTTAAGAAAATATGATAGCATCTTGTTCTTAGTCTTTTTCTTAATA
　　　　　　　　　　　　　　　　　　　　　ARE-1

GGGACATAAAGCCCACAAATAAAAATATGCCTGAAGAATGGGACAGGCATTGG

GCATTGTCCATGCCTAGTAAAGTACTCCAAGAACCTATTTGTATACTAGATGACA
　　　　　　　　　　ARE-2

CAATGTCAATGTCTGTGTACAACTGCCAACTGGGATGCAAGACACTGCCCATG

+1
CCAATCATCCTGAAAAGCAGGTATAAAAAGCAGGAAGCTACTCTGCACGTT
CAAT box　　　　　　　　　　　　　TATAA box
　　　　　　　　　　　　　　　　　　　　　　　　Transcription site
+28
GTCAGTGAGGTCCAGATACCTACAG-3'

FIGURE 10
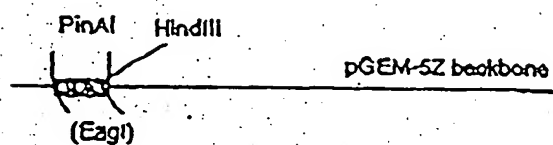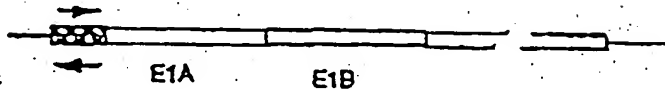
FIGURE 11

-3387

-3643

350 bp

-3993

1.8 kb

1.17 kb

-4814

-5155

ARE

-324 +33

Mini-promoter

FIGURE 12

CN749   hKLK2 P

CN702   E1A   E1B

CN763   hKLK2
         (1.8 kb E + P)

CN768   hKLK2
         (1.17 kb E + P)
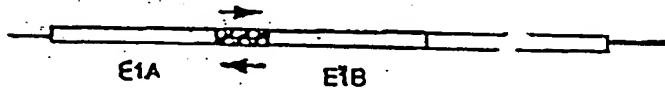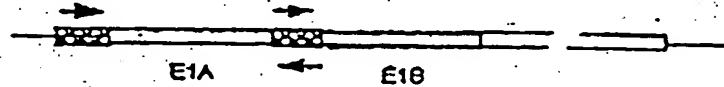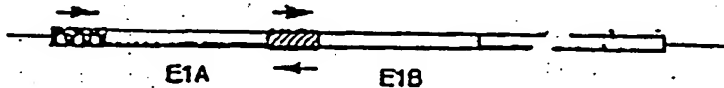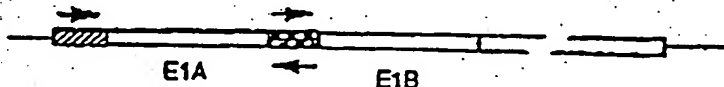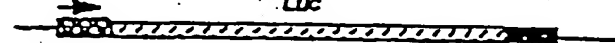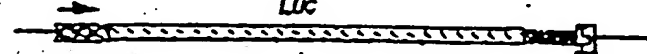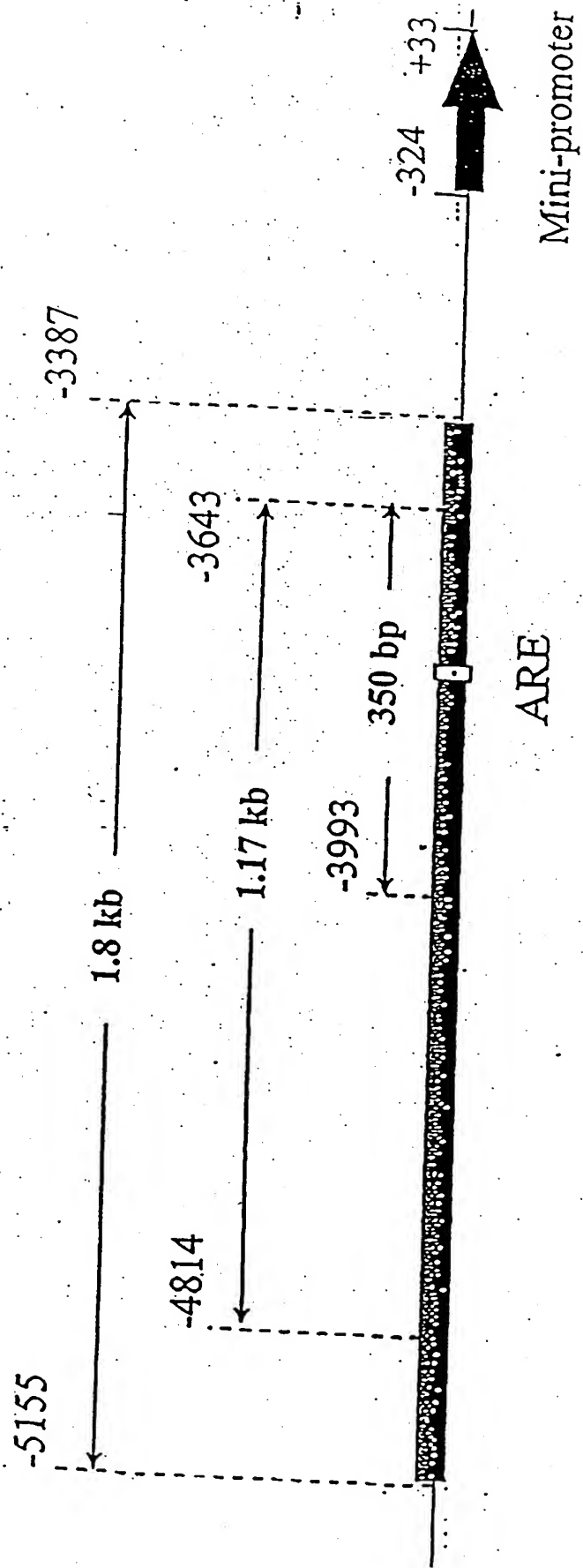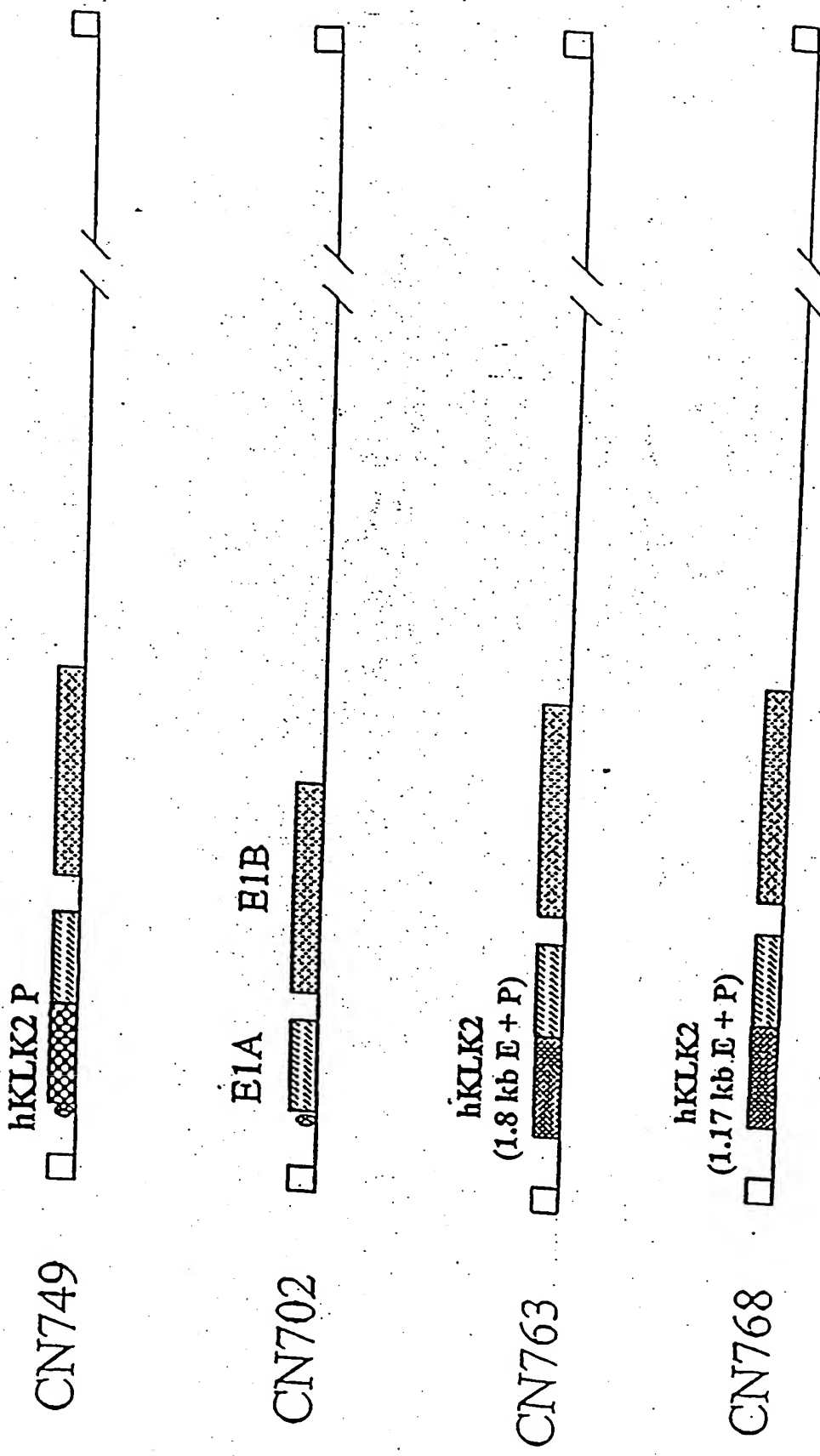
FIGURE 13

FIGURE 14A

```
aagctttta gtgctttaga cagtgagctg gtctgtctaa cccaagtgac ctgggctcca      60

tactcagccc cagaagtgaa gggtgaagct gggtggagcc aaaccaggca agcctaccct     120

cagggctccc agtggcctga gaaccattgg acccaggacc cattacttct agggtaagga     180

aggtacaaac accagatcca accatggtct gggggacag ctgtcaaatg cctaaaaata     240

tacctgggag aggagcaggc aaactatcac tgccccaggt tctctgaaca gaaacagagg     300

ggcaacccaa agtccaaatc caggtgagca ggtgcaccaa atgcccagag atatgacgag     360

gcaagaagtg aaggaaccac ccctgcatca aatgttttgc atgggaagga gaagggggtt     420

gctcatgttc ccaatccagg agaatgcatt tgggatctgc cttcttctca ctccttggtt     480

agcaagacta agcaaccagg actctggatt tggggaaaga cgtttatttg tggaggccag     540

tgatgacaat cccacgaggg cctaggtgaa gagggcagga aggctcgaga cactggggac     600

tgagtgaaaa ccacacccat gatctgcacc acccatggat gctccttcat tgctcacctt     660

tctgttgata tcagatggcc ccattttctg taccttcaca gaaggacaca ggctagggtc     720

tgtgcatggc cttcatcccc ggggccatgt gaggacagca ggtgggaaag atcatgggtc     780

ctcctgggtc ctgcagggcc agaacattca tcacccatac tgacctccta gatgggaatg     840

gcttccctgg ggctgggcca acggggcctg ggcaggggag aaaggacgtc aggggacagg     900

gaggaagggt catcgagacc cagcctggaa ggttcttgtc tctgaccatc caggatttac     960

ttccctgcat ctacctttgg tcattttccc tcagcaatga ccagctctgc ttcctgatct    1020

cagcctccca ccctggacac agcaccccag tccctggccc ggctgcatcc acccaatacc    1080

ctgataaccc aggacccatt acttctaggg taaggagggt ccaggagaca gaagctgagg    1140

aaaggtctga agaagtcaca tctgtcctgg ccagagggga aaaaccatca gatgctgaac    1200

caggagaatg ttgacccagg aaagggaccg aggacccaag aaaggagtca gaccaccagg    1260

gtttgcctga gaggaaggat caaggccccg agggaaagca gggctggctg catgtgcagg    1320

acactggtgg ggcatatgtg tcttagattc tccctgaatt cagtgtccct gccatggcca    1380

gactctctac tcaggcctgg acatgctgaa ataggacaat ggccttgtcc tctctcccca    1440

ccatttggca agagacataa aggacattcc aggacatgcc ttcctgggag gtccaggttc    1500

tctgtctcac acctcaggga ctgtagttac tgcatcagcc atggtaggtg ctgatctcac    1560

ccagcctgtc caggcccttc cactctccac tttgtgacca tgtccaggac caccctcag     1620

atcctgagcc tgcaaatacc cccttgctgg gtgggtggat tcagtaaaca gtgagctcct    1680
```
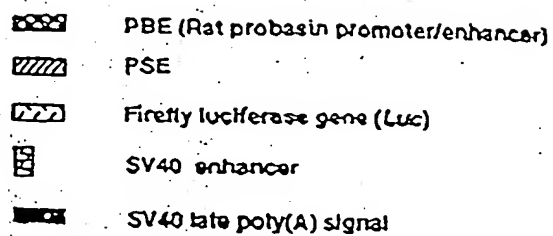
FIGURE 14B

```
atccagcccc cagagccacc tctgtcacct tcctgctggg catcatccca ccttcacaag    1740

cactaaagag catggggaga cctggctagc tgggtttctg catcacaaag aaaataatcc    1800

cccaggttcg gattcccagg gctctgtatg tggagctgac agacctgagg ccaggagata    1860

gcagaggtca gccctaggga gggtgggtca tccacccagg ggacaggggt gcaccagcct    1920

tgctactgaa agggcctccc caggacagcg ccatcagccc tgcctgagag ctttgctaaa    1980

cagcagtcag aggaggccat ggcagtggct gagctcctgc tccaggcccc aacagaccag    2040

accaacagca caatgcagtc cttccccaac gtcacaggtc accaaaggga aactgaggtg    2100

ctacctaacc ttagagccat caggggagat aacagcccaa tttcccaaac aggccagttt    2160

caatcccatg acaatgacct ctctgctctc attcttccca aaataggacg ctgattctcc    2220

cccaccatgg atttctccct tgtcccggga gccttttctg cccctatga tctgggcact     2280

cctgacacac acctcctctc tggtgacata tcagggtccc tcactgtcaa gcagtccaga    2340

aaggacagaa ccttggacag cgcccatctc agcttcaccc ttcctccttc acagggttca    2400

gggcaaagaa taaatggcag aggccagtga gcccagagat ggtgacaggc agtgacccag    2460

gggcagatgc ctggagcagg agctggcggg gccacaggga gaaggtgatg caggaaggga    2520

aacccagaaa tgggcaggaa aggaggacac aggctctgtg gggctgcagc ccagggttgg    2580

actatgagtg tgaagccatc tcagcaagta aggccaggtc ccatgaacaa gagtgggagc    2640

acgtggcttc ctgctctgta tatggggtgg gggattccat gccccataga accagatggc    2700

cggggttcag atggagaagg agcaggacag gggatcccca ggataggagg accccagtgt    2760

ccccacccag gcaggtgact gatgaatggg catgcagggt cctcctgggc tgggctctcc    2820

ctttgtccct caggattcct tgaaggaaca tccggaagcc gaccacatct acctggtggg    2880

ttctggggag tccatgtaaa gccaggagct tgtgttgcta ggaggggtca tggcatgtgc    2940

tgggggcacc aaagagagaa acctgagggc aggcaggacc tggtctgagg aggcatggga    3000

gcccagatgg ggagatggat gtcaggaaag gctgccccat cagggagggt gatagcaatg    3060

gggggtctgt gggagtgggc acgtgggatt ccctgggctc tgccaagttc cctcccatag    3120

tcacaacctg gggacactgc ccatgaaggg gcgcctttgc ccagccagat gctgctggtt    3180

ctgcccatcc actaccctct ctgctccagc cactctgggt ctttctccag atgccctgga    3240

cagccctggc ctgggcctgt cccctgagag gtgttgggag aagctgagtc tctggggaca    3300

ctctcatcag agtctgaaag gcacatcagg aaacatccct ggtctccagg actaggcaat    3360
```

FIGURE 14C

```
gaggaaaggg ccccagctcc tccctttgcc actgagaggg tcgaccctgg gtggccacag    3420

tgacttctgc gtctgtccca gtcaccctga aaccacaaca aaaccccagc cccagaccct    3480

gcaggtacaa tacatgtggg gacagtctgt acccagggga agccagttct ctcttcctag    3540

gagaccgggc ctcagggctg tgcccggggc aggcgggggc agcacgtgcc tgtccttgag    3600

aactcgggac cttaagggtc tctgctctgt gaggcacagc aaggatcctt ctgtccagag    3660

atgaaagcag ctcctgcccc tcctctgacc tcttcctcct tcccaaatct caaccaacaa    3720

ataggtgttt caaatctcat catcaaatct tcatccatcc acatgagaaa gcttaaaacc    3780

caatggattg acaacatcaa gagttggaac aagtggacat ggagatgtta cttgtggaaa    3840

tttagatgtg ttcagctatc gggcaggaga atctgtgtca aattccagca tggttcagaa    3900

gaatcaaaaa gtgtcacagt ccaaatgtgc aacagtgcag gggataaaac tgtggtgcat    3960

tcaaactgag ggatattttg gaacatgaga aaggaaggga ttgctgctgc acagaacatg    4020

gatgatctca cacatagagt tgaaagaaag gagtcaatcg cagaatagaa aatgatcact    4080

aattccacct ctataaagtt tccaagagga aaacccaatt ctgctgctag agatcagaat    4140

ggaggtgacc tgtgccttgc aatggctgtg agggtcacgg gagtgtcact tagtgcaggc    4200

aatgtgccgt atcttaatct gggcagggct ttcatgagca cataggaatg cagacattac    4260

tgctgtgttc attttacttc accggaaaag aagaataaaa tcagccgggc gcggtggctc    4320

acgcctgtaa tcccagcact ttagaaggct gaggtgggca gattacttga ggtcaggagt    4380

tcaagaccac cctggccaat atggtgaaac cccggctcta ctaaaaatac aaaaattagc    4440

tgggcatggt ggtgcgcgcc tgtaatccca gctactcggg aggctgaggc tggacaattg    4500

cttggaccca ggaagcagag gttgcagtga gccaagattg tgccactgca ctccagcttg    4560

ggcaacagag ccagactctg taaaaaaaaa aaaaaaaaa aaaaaagaa agaaagaaaa    4620

agaaagaaa gtataaaatc tctttgggtt aacaaaaaaa gatccacaaa acaaacacca    4680

gctcttatca aacttacaca actctgccag agaacaggaa acacaaatac tcattaactc    4740

acttttgtgg caataaaacc ttcatgtcaa aaggagacca ggacacaatg aggaagtaaa    4800

actgcaggcc ctacttgggt gcagagaggg aaaatccaca aataaaacat taccagaagg    4860

agctaagatt tactgcattg agttcattcc ccaggtatgc aaggtgattt taacacctga    4920

aaatcaatca ttgcctttac tacatagaca gattagctag aaaaaaatta caactagcag    4980

aacagaagca atttggcctt cctaaaattc cacatcatat catcatgatg gagacagtgc    5040

agacgccaat gacaataaaa agagggacct ccgtcacccg gtaaacatgt ccacacagct    5100
```

FIGURE 14D

```
ccagcaagca cccgtcttcc cagtgaatca ctgtaacctc ccctttaatc agccccaggc    5160

aaggctgcct gcgatggcca cacaggctcc aacccgtggg cctcaacctc ccgcagaggc    5220

tctcctttgg ccaccccatg gggagagcat gaggacaggg cagagccctc tgatgcccac    5280

acatggcagg agctgacgcc agagccatgg gggctggaga gcagagctgc tggggtcaga    5340

gcttcctgag gacacccagg cctaagggaa ggcagctccc tggatggggg caaccaggct    5400

ccgggctcca acctcagagc ccgcatggga ggagccagca ctctaggcct ttcctagggt    5460

gactctgagg ggaccctgac acgacaggat cgctgaatgc acccgagatg aaggggccac    5520

cacgggaccc tgctctcgtg gcagatcagg agagagtggg acaccatgcc aggcccccat    5580

ggcatggctg cgactgaccc aggccactcc cctgcatgca tcagcctcgg taagtcacat    5640

gaccaagccc aggaccaatg tggaaggaag gaaacagcat cccctttagt gatggaaccc    5700

aaggtcagtg caaagagagg ccatgagcag ttaggaaggg tggtccaacc tacagcacaa    5760

accatcatct atcataagta gaagccctgc tccatgaccc ctgcatttaa ataaacgttt    5820

gttaaatgag tcaaattccc tcaccatgag agctcacctg tgtgtaggcc catcacacac    5880

acaaacacac acacacac acacacacac acacacacac acagggaaag tgcaggatcc    5940

tggacagcac caggcaggct tcacaggcag agcaaacagc gtgaatgacc catgcagtgc    6000

cctgggcccc atcagctcag agaccctgtg agggctgaga tggggctagg caggggagag    6060

acttagagag ggtggggcct ccagggaggg ggctgcaggg agctgggtac tgccctccag    6120

ggaggggggct gcagggagct gggtactgcc ctccagggag ggggctgcag ggagctgggt    6180

actgccctcc agggaggggg ctgcagggag ctgggtactg ccctccaggg aggggggctgc    6240

agggagctgg gtactgccct ccagggaggc aggagcactg ttcccaacag agagcacatc    6300

ttcctgcagc agctgcacag acacaggagc ccccatgact gccctgggcc agggtgtgga    6360

ttccaaattt cgtgccccat tgggtgggac ggaggttgac cgtgacatcc aaggggcatc    6420

tgtgattcca aacttaaact actgtgccta caaaatagga aataaccctа ctttttctac    6480

tatctcaaat tccctaagca caagctagca cccttтaaat caggaagttc agtcactcct    6540

ggggtcctcc catgccccca gtctgacttg caggtgcaca gggtggctga catctgtcct    6600

tgctcctcct cttggctcaa ctgccgcccc tcctgggggt gactgatggt caggacaagg    6660

gatcctagag ctggccccat gattgacagg aaggcaggac ttggcctcca ttctgaagac    6720

taggggtgtc aagagagctg ggcatcccac agagctgcac aagatgacgc ggacagaggg    6780
```

FIGURE 14E

```
tgacacaggg ctcagggctt cagacgggtc gggaggctca gctgagagtt cagggacaga      6840

cctgaggagc ctcagtggga aaagaagcac tgaagtggga agttctggaa tgttctggac      6900

aagcctgagt gctctaagga aatgctccca ccccgatgta gcctgcagca ctggacggtc      6960

tgtgtacctc cccgctgccc atcctctcac agcccccgcc tctagggaca caactcctgc      7020

cctaacatgc atctttcctg tctcattcca cacaaaaggg cctctggggt ccctgttctg      7080

cattgcaagg agtggaggtc acgttcccac agaccaccca gcaacagggt cctatggagg      7140

tgcggtcagg aggatcacac gtccccccat gcccaggga ctgactctgg gggtgatgga      7200

ttggcctgga ggccactggt cccctctgtc cctgaggga atctgcaccc tggaggctgc      7260

cacatccctc ctgattcttt cagctgaggg cccttcttga aatcccaggg aggactcaac      7320

ccccactggg aaaggcccag tgtggacggt tccacagcag cccagctaag gcccttggac      7380

acagatcctg agtgagagaa cctttaggga cacaggtgca cggccatgtc cccagtgccc      7440

acacagagca ggggcatctg gaccctgagt gtgtagctcc cgcgactgaa cccagccctt      7500

ccccaatgac gtgacccctg gggtggctcc aggtctccag tccatgccac caaaatctcc      7560

agattgaggg tcctcccttg agtccctgat gcctgtccag gagctgcccc ctgagcaaat      7620

ctagagtgca gagggctggg attgtggcag taaaagcagc cacatttgtc tcaggaagga      7680

aagggaggac atgagctcca ggaagggcga tggcgtcctc tagtgggcgc ctcctgttaa      7740

tgagcaaaaa ggggccagga gagttgagag atcagggctg gccttggact aaggctcaga      7800

tggagaggac tgaggtgcaa agaggggct gaagtagggg agtggtcggg agagatggga      7860

ggagcaggta aggggaagcc ccagggaggc cggggaggg tacagcagag ctctccactc      7920

ctcagcattg acatttgggg tggtcgtgct agtggggttc tgtaagttgt agggtgttca      7980

gcaccatctg gggactctac ccactaaatg ccagcaggac tccctcccca agctctaaca      8040

accaacaatg tctccagact ttccaaatgt cccctggaga gcaaaattgc ttctggcaga      8100

atcactgatc tacgtcagtc tctaaaagtg actcatcagc gaaatccttc acctcttggg      8160

agaagaatca caagtgtgag aggggtagaa actgcagact tcaaaatctt tccaaaagag      8220

ttttacttaa tcagcagttt gatgtcccag gagaagatac atttagagtg tttagagttg      8280

atgccacatg gctgcctgta cctcacagca ggagcagagt gggttttcca agggcctgta      8340

accacaactg gaatgacact cactgggtta cattacaaag tggaatgtgg ggaattctgt      8400

agactttggg aagggaaatg tatgacgtga gcccacagcc taaggcagtg gacagtccac      8460

tttgaggctc tcaccatcta ggagacatct cagccatgaa catagccaca tctgtcatta      8520
```

FIGURE 14F

```
gaaaacatgt tttattaaga ggaaaaatct aggctagaag tgctttatgc tcttttttct      8580

ctttatgttc aaattcatat acttttagat cattccttaa agaagaatct atcccccctaa     8640

gtaaatgtta tcactgactg gatagtgttg gtgtctcact cccaacccct gtgtggtgac      8700

agtgccctgc ttccccagcc ctgggccctc tctgattcct gagagctttg ggtgctcctt      8760

cattaggagg aagagaggaa gggtgttttt aatattctca ccattcaccc atccacctct      8820

tagacactgg gaagaatcag ttgcccactc ttggatttga tcctcgaatt aatgacctct      8880

atttctgtcc cttgtccatt tcaacaatgt gacaggccta agaggtgcct tctccatgtg      8940

atttttgagg agaaggttct caagataagt tttctcacac ctctttgaat tacctccacc      9000

tgtgtcccca tcaccattac cagcagcatt tggaccctt ttctgttagt cagatgcttt        9060

ccacctcttg agggtgtata ctgtatgctc tctacacagg aatatgcaga ggaaatagaa      9120

aaagggaaat cgcattacta ttcagagaga agaagacctt tatgtgaatg aatgagagtc      9180

taaaatccta agagagccca tataaaatta ttaccagtgc taaaactaca aaagttacac      9240

taacagtaaa ctagaataat aaaacatgca tcacagttgc tggtaaagct aaatcagata      9300

tttttttctt agaaaaagca ttccatgtgt gttgcagtga tgacaggagt gcccttcagt      9360

caatatgctg cctgtaattt ttgttccctg gcagaatgta ttgtcttttc tccctttaaa      9420

tcttaaatgc aaaactaaag gcagctcctg ggccccctcc ccaaagtcag ctgcctgcaa      9480

ccagccccac gaagagcaga ggcctgagct tccctggtca aaatagggg ctagggagct        9540

taaccttgct cgataaagct gtgttcccag aatgtcgctc ctgttcccag gggcaccagc      9600

ctggagggtg gtgagcctca ctggtggcct gatgcttacc ttgtgccctc acaccagtgg      9660

tcactggaac cttgaacact tggctgtcgc ccggatctgc agatgtcaag aacttctgga      9720

agtcaaatta ctgcccactt ctccagggca gatacctgtg aacatccaaa accatgccac      9780

agaaccctgc ctggggtcta caacacatat ggactgtgag caccaagtcc agccctgaat      9840

ctgtgaccac ctgccaagat gcccctaact gggatccacc aatcactgca catggcaggc      9900

agcgaggctt ggaggtgctt cgccacaagg cagccccaat ttgctgggag tttcttggca      9960

cctggtagtg gtgaggagcc ttgggaccct caggattact ccccttaagc atagtgggga     10020

cccttctgca tccccagcag gtgccccgct cttcagagcc tctctctctg aggtttaccc     10080

agacccctgc accaatgaga ccatgctgaa gcctcagaga gagagatgga gctttgacca     10140

ggagccgctc ttccttgagg gccagggcag ggaaagcagg aggcagcacc aggagtggga     10200
```

```
acaccagtgt ctaagcccct gatgagaaca gggtggtctc tcccatatgc ccataccagg    10260

cctgtgaaca gaatcctcct tctgcagtga caatgtctga gaggacgaca tgtttcccag    10320

cctaacgtgc agccatgccc atctacccac tgcctactgc aggacagcac caacccagga    10380

gctgggaagc tgggagaaga catggaatac ccatggcttc tcaccttcct ccagtccagt    10440

gggcaccatt tatgcctagg acacccacct gccggcccca ggctcttaag agttaggtca    10500

cctaggtgcc tctgggaggc cgaggcagga gaattgcttg aacccgggag gcagaggttg    10560

cagtgagccg agatcacacc actgcactcc agcctgggtg acagaatgag actctgtctc    10620

aaaaaaaaag agaaagatag catcagtggc taccaagggc tagggcagg ggaggtgga     10680

gagttaatga ttaatagtat gaagtttcta tgtgagatga tgaaaatgtt ctggaaaaaa    10740

aaatatagtg gtgaggatgt agaatattgt gaatataatt aacggcattt aattgtacac    10800

ttaacatgat taatgtggca tattttatct tatgtatttg actacatcca agaaacactg    10860

ggagagggaa agcccaccat gtaaaataca cccaccctaa tcagatagtc ctcattgtac    10920

ccaggtacag gcccctcatg acctgcacag gaataactaa ggatttaagg acatgaggct    10980

tcccagccaa ctgcaggtgc acaacataaa tgtatctgca aacagactga gagtaaagct    11040

gggggcacaa acctcagcac tgccaggaca cacacccttc tcgtggattc tgactttatc    11100

tgacccggcc cactgtccag atcttgttgt gggattggga caagggaggt cataaagcct    11160

gtccccaggg cactctgtgt gagcacacga gacctcccca ccccccacc gttaggtctc    11220

cacacataga tctgaccatt aggcattgtg aggaggactc tagcgcgggc tcagggatca    11280

caccagagaa tcaggtacag agaggaagac ggggctcgag gagctgatgg atgacacaga    11340

gcagggttcc tgcagtccac aggtccagct caccctggtg taggtgcccc atcccctga    11400

tccaggcatc cctgacacag ctccctcccg gagcctcctc ccaggtgaca catcagggtc    11460

cctcactcaa gctgtccaga gagggcagca ccttggacag cgcccacccc acttcactct    11520

tcctccctca cagggctcag ggctcagggc tcaagtctca gaacaaatgg cagaggccag    11580

tgagcccaga gatggtgaca gggcaatgat ccaggggcag ctgcctgaaa cgggagcagg    11640

tgaagccaca gatgggagaa gatggttcag caagaaaaat ccaggaatgg gcaggagagg    11700

agaggaggac acaggctctg tggggctgca ccccaggatg ggactaagtg tgaagacatc    11760

tcagcaggtg aggccaggtc ccatgaacag agaagcagct cccacctccc ctgatgcacg    11820

gacacacaga gtgtgtggtg ctgtgccccc agagtcgggc tctcctgttc tggtccccag    11880

ggagtgagaa gtgaggttga cttgtccctg ctcctctctg ctaccccaac attcaccttc    11940
```

FIGURE 14H

```
tcctcatgcc cctctctctc aaatatgatt tggatctatg tccccgccca aatctcatgt    12000

caaattgtaa accccaatgt tggaggtggg gccttgtgag aagtgattgg ataatgcggg    12060

tggattttct gctttgatgc tgtttctgtg atagagatct cacatgatct ggttgtttaa    12120

aagtgtgtag cacctctccc ctctctctct ctctctctta ctcatgctct gccatgtaag    12180

acgttcctgt ttccccttca ccgtccagaa tgattgtaag ttttctgagg cctccccagg    12240

agcagaagcc actatgcttc ctgtacaact gcagaatgat gagcgaatta aacctctttt    12300

ctttataaat tacccagtct caggtatttc tttatagcaa tgcgaggaca gactaataca    12360

atcttctact cccagatccc cgcacacgct tagccccaga catcactgcc cctgggagca    12420

tgcacagcgc agcctcctgc cgacaaaagc aaagtcacaa aaggtgacaa aaatctgcat    12480

ttggggacat ctgattgtga aagagggagg acagtacact tgtagccaca gagactgggg    12540

ctcaccgagc tgaaacctgg tagcactttg gcataacatg tgcatgaccc gtgttcaatg    12600

tctagagatc agtgttgagt aaaacagcct ggtctggggc cgctgctgtc cccacttccc    12660

tcctgtccac cagagggcgg cagagttcct cccaccctgg agcctcccca ggggctgctg    12720

acctccctca gccgggccca cagcccagca gggtccaccc tcacccgggt cacctcggcc    12780

cacgtcctcc tcgccctccg agctcctcac acggactctg tcagctcctc cctgcagcct    12840

atcggccgcc cacctgaggc ttgtcggccg cccacttgag gcctgtcggc tgccctctgc    12900

aggcagctcc tgtcccctac acccctcct tccccgggct cagctgaaag ggcgtctccc    12960

agggcagctc cctgtgatct ccaggacagc tcagtctctc acaggctccg acgcccccta    13020

tgctgtcacc tcacagccct gtcattacca ttaactcctc agtcccatga agttcactga    13080

gcgcctgtct cccggttaca ggaaaactct gtgacaggga ccacgtctgt cctgctctct    13140

gtggaatccc agggcccagc ccagtgcctg acacggaaca gatgctccat aaatactggt    13200

taaatgtgtg ggagatctct aaaaagaagc atatcacctc cgtgtggccc ccagcagtca    13260

gagtctgttc catgtggaca caggggcact ggcaccagca tgggaggagg ccagcaagtg    13320

cccgcggctg ccccaggaat gaggcctcaa cccccagagc ttcagaaggg aggacagagg    13380

cctgcaggga atagatcctc cggcctgacc ctgcagccta atccagagtt cagggtcagc    13440

tcacaccacg tcgaccctgg tcagcatccc tagggcagtt ccagacaagg ccggaggtct    13500

cctcttgccc tccagggggt gacattgcac acagacatca ctcaggaaac ggattcccct    13560

ggacaggaac ctggctttgc taaggaagtg gaggtggagc ctggtttcca tcccttgctc    13620
```

FIGURE 14I

```
caacagaccc ttctgatctc tcccacatac ctgctctgtt cctttctggg tcctatgagg    13680

accctgttct gccaggggtc cctgtgcaac tccagactcc ctcctggtac caccatgggg    13740

aaggtggggt gatcacagga cagtcagcct cgcagagaca gagaccaccc aggactgtca    13800

gggagaacat ggacaggccc tgagccgcag ctcagccaac agacacggag agggagggtc    13860

cccctggagc cttccccaag gacagcagag cccagagtca cccacctccc tccaccacag    13920

tcctctcttt ccaggacaca caagacacct cccccctccac atgcaggatc tggggactcc    13980

tgagacctct gggcctgggt ctccatccct gggtcagtgg cggggttggt ggtactggag    14040

acagagggct ggtccctccc cagccaccac ccagtgagcc tttttctagc ccccagagcc    14100

acctctgtca ccttcctgtt gggcatcatc ccaccttccc agagccctgg agagcatggg    14160

gagacccggg accctgctgg gtttctctgt cacaaaggaa aataatcccc ctggtgtgac    14220

agacccaagg acagaacaca gcagaggtca gcactgggga agacaggttg tcctcccagg    14280

ggatgggggt ccatccacct tgccgaaaag atttgtctga ggaactgaaa atagaaggga    14340

aaaaagagga gggacaaaag aggcagaaat gagaggggag gggacagagg acacctgaat    14400

aaagaccaca cccatgaccc acgtgatgct gagaagtact cctgccctag gaagagactc    14460

agggcagagg gaggaaggac agcagaccag acagtcacag cagccttgac aaaacgttcc    14520

tggaactcaa gctcttctcc acagaggagg acagagcaga cagcagagac catggagtct    14580

ccctcggccc ctccccacag atggtgcatc ccctggcaga ggctcctgct cacaggtgaa    14640

gggaggacaa cctgggagag ggtgggagga gggagctggg gtctcctggg taggacaggg    14700

ctgtgagacg gacagagggc tcctgttgga gcctgaatag ggaagaggac atcagagagg    14760

gacaggagtc acaccagaaa aatcaaattg aactggaatt ggaaaggggc aggaaaacct    14820

caagagttct attttcctag ttaattgtca ctggccacta cgtttttaaa aatcataata    14880

actgcatcag atgacacttt aaataaaaac ataaccaggg catgaaacac tgtcctcatc    14940

cgcctaccgc ggacattgga aaataagccc caggctgtgg agggccctgg gaaccctcat    15000

gaactcatcc acaggaatct gcagcctgtc ccaggcactg gggtgcaacc aagatc        15056
```

FIGURE 15A

```
aagcttctag ttttcttttc ccggtgacat cgtggaaagc actagcatct ctaagcaatg 60

atctgtgaca atattcacag tgtaatgcca tccagggaac tcaactgagc cttgatgtcc 120

agagattttt gtgttttttt ctgagactga gtctcgctct gtgccaggct ggagtgcagt 180

ggtgcaacct tggctcactg caagctccgc ctcctgggtt cacgccattc tcctgcctca 240

gcctcctgag tagctgggac tacaggcacc cgccaccacg cctggctaat ttttttgtat 300

ttttagtaga gatggggttt cactgtgtta gccaggatgg tctcagtctc ctgacctcgt 360

gatctgccca ccttggcctc ccaaagtgct gggatgacag gcgtgagcca ccgcgcctgg 420

ccgatatcca gagatttttt gggggctcc atcacacaga catgttgact gtcttcatgg 480

ttgactttta gtatccagcc cctctagaaa tctagctgat atagtgtggc tcaaaacctt 540

cagcacaaat cacaccgtta gactatctgg tgtggcccaa accttcaggt gaacaaaggg 600

actctaatct ggcaggatat tccaaagcat tagagatgac ctcttgcaaa gaaaaagaaa 660

tggaaaagaa aaagaaagaa aggaaaaaaa aaaaaaaaaa gagatgacct ctcaggctct 720

gaggggaaac gcctgaggtc tttgagcaag gtcagtcctc tgttgcacag tctccctcac 780

agggtcattg tgacgatcaa atgtggtcac gtgtatgagg caccagcaca tgcctggctc 840

tggggagtgc cgtgtaagtg tatgcttgca ctgctgaatg cttgggatgt gtcagggatt 900

atcttcagca cttacagatg ctcatctcat cctcacagca tcactatggg atgggtatta 960

ctggcctcat ttgatggaga aagtggctgt ggctcagaaa gggggggacca ctagaccagg 1020

gacactctgg atgctgggga ctccagagac catgaccact caccaactgc agagaaatta 1080

attgtggcct gatgtccctg tcctggagag ggtggaggtg gaccttcact aacctcctac 1140

cttgaccctc tcttttaggg ctctttctga cctccaccat ggtactagga ccccattgta 1200

ttctgtaccc tcttgactct atgaccccca ctgcccactg catccagctg ggtcccctcc 1260

tatctctatt cccagctggc cagtgcagtc tcagtgccca cctgtttgtc agtaactctg 1320

aaggggctga cattttactg acttgcaaac aaataagcta actttccaga gttttgtgaa 1380

tgctggcaga gtccatgaga ctcctgagtc agaggcaaag gcttttactg ctcacagctt 1440

agcagacagc atgaggttca tgttcacatt agtacacctt gcccccccca aatcttgtag 1500

ggtgaccaga gcagtctagg tggatgctgt gcagaagggg tttgtgccac tggtgagaaa 1560

cctgagatta ggaatcctca atcttatact gggacaactt gcaaacctgc tcagcctttg 1620

tctctgatga agatattatc ttcatgatct tggattgaaa acagacctac tctggaggaa 1680
```

FIGURE 15B

```
catattgtat cgattgtcct tgacagtaaa caaatctgtt gtaagagaca ttatctttat 1740

tatctaggac agtaagcaag cctggatctg agagagatat catcttgcaa ggatgcctgc 1800

tttacaaaca tccttgaaac aacaatccag aaaaaaaaag gtgttgctgt ctttgctcag 1860

aagacacaca gatacgtgac agaaccatgg agaattgcct cccaacgctg ttcagccaga 1920

gccttccacc cttgtctgca ggacagtctc aacgttccac cattaaatac ttcttctatc 1980

acatcctgct tctttatgcc taaccaaggt tctaggtccc gatcgactgt gtctggcagc 2040

actccactgc caaacccaga ataaggcagc gctcaggatc ccgaaggggc atggctgggg 2100

atcagaactt ctgggtttga gtgaggagtg ggtccaccct cttgaatttc aaaggaggaa 2160

gaggctggat gtgaaggtac tgggggaggg aaagtgtcag ttccgaactc ttaggtcaat 2220

gagggaggag actggtaagg tcccagctcc cgaggtactg atgtgggaat ggcctaagaa 2280

tctcatatcc tcaggaagaa ggtgctggaa tcctgagggg tagagttctg ggtatatttg 2340

tggcttaagg ctctttggcc cctgaaggca gaggctggaa ccattaggtc cagggtttgg 2400

ggtgatagta atgggatctc ttgattcctc aagagtctga ggatcgaggg ttgcccattc 2460

ttccatcttg ccacctaatc cttactccac ttgagggtat caccagccct tctagctcca 2520

tgaaggtccc ctgggcaagc acaatctgag catgaaagat gccccagagg ccttgggtgt 2580

catccactca tcatccagca tcacactctg agggtgtggc cagcaccatg acgtcatgtt 2640

gctgtgacta tccctgcagc gtgcctctcc agccacctgc caaccgtaga gctgcccatc 2700

ctcctctggt gggagtggcc tgcatggtgc caggctgagg cctagtgtca gacagggagc 2760

ctggaatcat agggatccag gactcaaaag tgctagagaa tggccatatg tcaccatcca 2820

tgaaatctca agggcttctg ggtggagggc acaggacct gaacttatgg tttcccaagt 2880

ctattgctct cccaagtgag tctcccagat acgaggcact gtgccagcat cagccttatc 2940

tccaccacat cttgtaaaag gactacccag ggccctgatg aacaccatgg tgtgtacagg 3000

agtaggggt ggaggcacgg actcctgtga ggtcacagcc aaggagcat catcatgggt 3060

ggggaggagg caatggacag gcttgagaac ggggatgtgg ttgtatttgg ttttctttgg 3120

ttagataaag tgctgggtat aggattgaga gtggagtatg aagaccagtt aggatggagg 3180

atcagattgg agttgggtta gataaagtgc tgggtatagg attgagagtg gagtatgaag 3240

accagttagg atggaggatc agattggagt tgggttagag atggggtaaa attgtgctcc 3300

ggatgagttt gggattgaca ctgtggaggt ggtttgggat ggcatggctt tgggatggaa 3360
```

```
atagatttgt tttgatgttg gctcagacat ccttggggat tgaactgggg atgaagctgg 3420

gtttgatttt ggaggtagaa gacgtggaag tagctgtcag atttgacagt ggccatgagt 3480

tttgtttgat ggggaatcaa acaatggggg aagacataag ggttggcttg ttaggttaag 3540

ttgcgttggg ttgatggggt cggggctgtg tataatgcag ttggattggt ttgtattaaa 3600

ttgggttggg tcaggttttg gttgaggatg agttgaggat atgcttgggg acaccggatc 3660

catgaggttc tcactggagt ggagacaaac ttcctttcca ggatgaatcc agggaagcct 3720

taattcacgt gtaggggagg tcaggccact ggctaagtat atccttccac tccagctcta 3780

agatggtctt aaattgtgat tatctatatc cacttctgtc tccctcactg tgcttggagt 3840

ttacctgatc actcaactag aaacagggga agatttatc aaattctttt ttttttttt 3900

ttttttttga gacagagtct cactctgttg cccaggctgg agtgcagtgg cgcagtctcg 3960

gctcactgca acctctgcct cccaggttca agtgattctc ctgcctcagc ctcctgagtt 4020

gctgggatta caggcatgca gcaccatgcc cagctaattt ttgtattttt agtagagatg 4080

gggtttcacc aatgtttgcc aggctggcct cgaactcctg acctggtgat ccacctgcct 4140

cagcctccca aagtgctggg attacaggcg tcagccaccg cgcccagcca cttttgtcaa 4200

attcttgaga cacagctcgg gctggatcaa gtgagctaet ctggttttat tgaacagctg 4260

aaataaccaa ctttttggaa attgatgaaa tcttacggag ttaacagtgg aggtaccagg 4320

gctcttaaga gttcccgatt ctcttctgag actacaaatt gtgattttgc atgccacctt 4380

aatctttttt tttttttttt taaatcgagg tttcagtctc attctatttc ccaggctgga 4440

gttcaatagc gtgatcacag ctcactgtag ccttgaactc ctggccttaa gagattctcc 4500

tgcttcggtc tcccaatagc taagactaca gtagtccacc accatatcca gataattttt 4560

aaatttttg gggggccggg cacagtggct cacgcctgta atcccaacac catgggaggc 4620

tgagatgggt ggatcacgag gtcaggagtt tgagaccagc ctgaccaaca tggtgaaact 4680

ctgtctctac taaaaaaaaa aaaatagaa aaattagccg ggcgtggtgg cacacggcac 4740

ctgtaatccc agctactgag gaggctgagg caggagaatc acttgaaccc agaaggcaga 4800

ggttgcaatg agccgagatt gcgccactgc actccagcct gggtgacaga gtgagactct 4860

gtctcaaaaa aaaaaattt tttttttttt tttgtagaga tggatcttgc tttgtttctc 4920

tggttggcct tgaactcctg gcttcaagtg atcctcctac cttggcctcg gaaagtgttg 4980

ggattacagg cgtgagccac catgactgac ctgtcgttaa tcttgaggta cataaacctg 5040

gctcctaaag gctaaaggct aaatatttgt tggagaaggg gcattggatt ttgcatgagg 5100
```

FIGURE 15D

```
atgattctga cctgggaggg caggtcagca ggcatctctg ttgcacagat agagtgtaca 5160

ggtctggaga acaaggagtg gggggttatt ggaattccac attgtttgct gcacgttgga 5220

ttttgaaatg ctagggaact ttgggagact catatttctg ggctagagga tctgtggacc 5280

acaagatctt tttatgatga cagtagcaat gtatctgtgg agctggattc tgggttggga 5340

gtgcaaggaa aagaatgtac taaatgccaa gacatctatt tcaggagcat gaggaataaa 5400

agttctagtt tctggtctca gagtggtgca gggatcaggg agtctcacaa tctcctgagt 5460

gctggtgtct tagggcacac tgggtcttgg agtgcaaagg atctaggcac gtgaggcttt 5520

gtatgaagaa tcggggatcg tacccacccc ctgtttctgt ttcatcctgg gcatgtctcc 5580

tctgcctttg tcccctagat gaagtctcca tgagctacaa gggcctggtg catccagggt 5640

gatctagtaa ttgcagaaca gcaagtgcta gctctccctc cccttccaca gctctgggtg 5700

tgggaggggg ttgtccagcc tccagcagca tggggagggc cttggtcagc ctctgggtgc 5760

cagcagggca ggggcggagt cctggggaat gaaggtttta tagggctcct gggggaggct 5820

ccccagcccc aagctt                                                  5836
```

FIGURE 16A

```
gaattcagaa ataggggaag gttgaggaag gacactgaac tcaaaggggga tacagtgatt 60

ggtttatttg tcttctcttc acaacattgg tgctggagga attcccaccc tgaggttatg 120

aagatgtctg aacacccaac acatagcact ggagatatga gctcgacaag agtttctcag 180

ccacagagat tcacagccta gggcaggagg acactgtacg ccaggcagaa tgacatggga 240

attgcgctca cgattggctt gaagaagcaa ggactgtggg aggtgggctt tgtagtaaca 300

agagggcagg gtgaactctg attcccatgg gggaatgtga tggtcctgtt acaaattttt 360

caagctggca gggaataaaa cccattacgg tgaggacctg tggagggcgg ctgccccaac 420

tgataaagga aatagccagg tgggggcctt tcccattgta gggggacat atctggcaat 480

agaagccttt gagacccttt agggtacaag tactgaggca gcaaataaaa tgaaatctta 540

tttttcaact ttatactgca tgggtgtgaa gatatatttg tttctgtaca gggggtgagg 600

gaaaggaggg gaggaggaaa gttcctgcag gtctggtttg gtcttgtgat ccaggggggtc 660

ttggaactat ttaaattaaa ttaaattaaa acaagcgact gttttaaatt aaattaaatt 720

aaattaaatt ttactttatt ttatcttaag ttctgggcta catgtgcagg acgtgcagct 780

ttgttacata ggtaaacgtg tgccatggtg gtttgctgta cctatcaacc catcacctag 840

gtattaagcc cagcatgcat tagctgtttt tcctgacgct ctccctctcc ctgactccca 900

caacaggccc cagtgtgtgt tgttcccctc cctgtgtcca tgtgttctca ttgttcagct 960

cccacttata agtgagaaca tgtggtgttt ggttttctgt ttctgtgtta gtttgctgag 1020

gataatggct tccacctcca tccatgttcc tgcaaaggac gtgatcttat tcttttttat 1080

ggttgcatag aaattgtttt tacaaatcca attgatattg tatttaatta caagttaatc 1140

taattagcat actagaagag attacagaag atattaggta cattgaatga ggaaatatat 1200

aaaataggac gaaggtgaaa tattaggtag gaaaagtata atagttgaaa gaagtaaaaa 1260

aaaatatgca tgagtagcag aatgtaaaag aggtgaagaa cgtaatagtg acttttaga 1320

ccagattgaa ggacagagac agaaaaattt taaggaattg ctaaccatg tgagtgttag 1380

aagtacagtc aataacatta aagcctcagg aggagaaaag aatacgaaag gaggaaatat 1440

gtgaataaat agtagagaca tgtttgatgg attttaaaat atttgaaaga cctcacatca 1500

aaggattcat accgtgccat tgaagaggaa gatggaaaag ccaacaagcc agatgaaagt 1560

tagaaatatt attggcaaag cttaaatgtt aaaagtccta gagacaaagg atggcagaaa 1620

tattggcggg aaagaatgca gaacctagaa tataaattca tcccaacagt ttggtagtgt 1680
```

```
gcagctgtag cctttctag ataatacact attgtcatac atcgcttaag cgagtgtaaa 1740

atggtctcct cactttattt atttatatat ttatttagtt ttgagatgga gcctcgctct 1800

gtctcctagg ctggagtgca atagtgcgat accactcact gcaacctctg cctcctctgt 1860

tcaagtgatt ttcttacctc agcctcccga gtagctggga ttacaggtgc gtgccaccac 1920

acccggctaa tttttgtatt ttttgtagag acggggtttt gccatgttgg ccaggctggt 1980

cttgaactcc tgacatcagg tgatccacct gccttggcct cctaaagtgc tgggattaca 2040

ggcatgagcc accgtgccca accactttat ttattttta tttttatttt taaatttcag 2100

cttctatttg aaatacaggg ggcacatata taggattgtt acatgggtat attgaactca 2160

ggtagtgatc atactaccca acaggtaggt tttcaaccca ctccccctct tttcctcccc 2220

attctagtag tgtgcagtgt ctattgttct catgtttatg tctatgtgtg ctccaggttt 2280

agctcccacc tgtaagtgag aacgtgtggt atttgatttt ctgtccctgt gttaattcac 2340

ttaggattat ggcttccagc tccattcata ttgctgtaaa ggatatgatt catttttcat 2400

ggccatgcag tattccatat tgcgtataga tcacattttc tttcttttt ttttttgaga 2460

cggagtcttg ctttgctgcc taggctggag tgcagtagca cgatctcggc tcactgcaag 2520

cttcacctcc ggggttcacg tcattcttct gtctcagctt cccaagtagc tgggactaca 2580

ggcgcccgcc accacgtccg gctaattttt ttgtgtgttt ttagtagaga tggggtttc 2640

actgtgttag ccaggatggt cttgatctcc tgaccttgtg gtccacctgc ctcggtctcc 2700

caaagtgctg ggattacagg ggtgagccac tgcgcccggc ccatatatac cacattttct 2760

ttaaccaatc caccattgat gggcaactag gtagattcca tggattccac agttttgcta 2820

ttgtgtgcag tgtggcagta gacatatgaa tgaatgtgtc tttttggtat aatgatttgc 2880

attcctttgg gtatacagtc attaatagga gtgctgggtt gaacggtggc tctgtttaaa 2940

attctttgag aattttccaa actgtttgcc atagagagca aactaattta catttccacg 3000

aacagtatat aagcattccc ttttctccac agctttgtca tcatggtttt tttttttctt 3060

tattttaaaa aagaatatgt tgttgttttc ccagggtaca tgtgcaggat gtgcaggttt 3120

gttacatagg tagtaaacgt gagccatggt ggtttgctgc acctgtcaac ccattacctg 3180

ggtatgaagc cctgcctgca ttagctcttt tccctaatgc tctcactact gccccaccct 3240

caccctgaca gggcaaacag acaacctaca gaatgggagg aaattttgc aatctattca 3300

tctgacaaag gtcaagaata tccagaatct acaaggaact taagcaaatt tttacttttt 3360
```

FIGURE 16C

```
aataatagcc actctgactg gcgtgaaatg gtatctcatt gtggttttca tttgaatttc 3420

tctgatgatc agtgacgatg agcatttttt catatttgtt ggctgcttgt acgtcttttg 3480

agaagtgtct cttcatgcct tttggccact ttaatgggat tatttttttgc tttttagttt 3540

aagttcctta tagattctgg atattagact tcttattgga tgcatagttt gtgaatactc 3600

tcttccattc tgtaggttgt ctgtttactc tattgatggc ttcttttgct gtgccgaagc 3660

atcttagttt aattagaaac cacctgccaa tttttgtttt tgttgcaatt gcttttgggg 3720

acttagtcat aaactctttg ccaaggtctg ggtcaagaag agtatttcct aggttttctt 3780

ctagaatttt gaaagtctga atgtaaacat ttgcattttt aatgcatctt gagttagttt 3840

ttgtatatgt gaaaggtcta ctctcatttt ctttccctct ttctttcttt ctttcttttc 3900

tttctttctt tctttctttc tttctttctt tctttctttc tttctttttg tccttctttc 3960

tttctttctt tctctttctt tctctctttc tttttttttt ttgatggagt attgctctgt 4020

tgcccaggct gcagtgcagc ggcacgatct cggctcactg caacctctgc ctcctgggtt 4080

caactgattc tcctgcatca gccttccaag tagctgggat tataggcgcc cgccaccacg 4140

cccgactaat ttttgtattt ttagtagaga cggggttgtg ccatgttggc caggctggtt 4200

tgaaactcct gacctcaaac gatctgcctg ccttggcctc ccaaagtgct gggattacag 4260

gtgtgagcca ctgtgcccag ccaagaatgt cattttctaa gaggtccaag aacctcaaga 4320

tattttggga ccttgagaag agaggaattc atacaggtat tacaagcaca gcctaatggc 4380

aaatctttgg catggcttgg cttcaagact ttaggctctt aaaagtcgaa tccaaaaatt 4440

tttataaaag ctccagctaa gctaccttaa aaggggcctg tatggctgat cactcttctt 4500

gctatacttt acacaaataa acaggccaaa tataatgagg ccaaaattta ttttgcaaat 4560

aaattggtcc tgctatgatt tactcttggt aagaacaggg aaaatagaga aaaatttaga 4620

ttgcatctga ccttttttttc tgaattttta tatgtgccta caatttgagc taaatcctga 4680

attattttct ggttgcaaaa actctctaaa gaagaacttg gttttcattg tcttcgtgac 4740

acattatct ggctctttac tagaacagct ttcttgtttt tggtgttcta gcttgtgtgc 4800

cttacagttc tactcttcaa attattgtta tgtgtatctc atagttttcc ttcttttgag 4860

aaaactgaag ccatggtatt ctgaggacta gagatgactc aacagagctg gtgaatctcc 4920

tcatatgcaa tccactgggc tcgatctgct tcaaattgct gatgcactgc tgctaaagct 4980

atacatttaa aaccctcact aaaggatcag ggaccatcat ggaagaggag gaaacatgaa 5040

attgtaagag ccagattcgg ggggtagagt gtggaggtca gagcaactcc accttgaata 5100
```

FIGURE 16D

```
agaaggtaaa gcaacctatc ctgaaagcta acctgccatg gtggcttctg attaacctct 5160

gttctaggaa gactgacagt ttgggtctgt gtcattgccc aaatctcatg ttaaattgta 5220

atccccagtg ttcggaggtg ggacttggtg gtaggtgatt cggtcatggg agtagatttt 5280

cttctttgtg gtgttacagt gatagtgagt gagttctcgt gagatctggt catttaaaag 5340

tgtgtggccc ctcccctccc tctcttggtc ctcctactgc catgtaagat acctgctcct 5400

gctttgcctt ctaccataag taaaagcccc ctgaggcctc cccagaagca gatgccacca 5460

tgcttcctgt acagcctgca gaaccatcag ccaattaaac ctcttttctg tataaattac 5520

cagtcttgag tatctctttа cagcagtgtg agaacggact aatacaaggg tctccaaaat 5580

tccaagttta tgtattcttt cttgccaaat agcaggtatt taccataaat cctgtcctta 5640

ggtcaaacaa ccttgatggc atcgtacttc aattgtctta cacattcctt ctgaatgact 5700

cctccctat ggcatataag ccctgggtct tgggggataa tggcagaggg gtccaccatc 5760

ttgtctggct gccacctgag acacggacat ggcttctgtt ggtaagtctc tattaaatgt 5820

ttctttctaa gaaactggat ttgtcagctt gtttctttgg cctctcagct tcctcagact 5880

ttggggtagg ttgcacaacc ctgcccacca cgaaacaaat gtttaatatg ataaatatgg 5940

atagatataa tccacataaa taaaagctct tggagggccc tcaataattg ttaagagtgt 6000

aaatgtgtcc aaagatggaa aatgtttgag aactactgtc ccagagattt tcctgagttc 6060

tagagtgtgg gaatatagaa cctggagctt ggcttcttca gcctagaatc aggagtatgg 6120

ggctgaagtc tgaagcttgg cttcagcagt ttggggttgg cttccggagc acatatttga 6180

catgttgcga ctgtgatttg gggtttggta tttgctctga atcctaatgt ctgtccttga 6240

ggcatctaga atctgaaatc tgtggtcaga attctattat cttgagtagg acatctccag 6300

tcctggttct gccttctagg gctggagtct gtagtcagtg acccggtctg gcatttcaac 6360

ttcatataca gtgggctatc ttttggtcca tgtttcaacc aaacaaccga ataaaccatt 6420

agaacctttc cccacttccc tagctgcaat gttaaaccta ggatttctgt ttaataggtt 6480

catatgaata atttcagcct gatccaactt tacattcctt ctaccgttat tctacaccca 6540

ccttaaaaat gcattcccaa tatattccct ggattctacc tatatatggt aatcctggct 6600

ttgccagttt ctagtgcatt aacatacctg atttacattc ttttacttta aagtggaaat 6660

aagagtccct ctgcagagtt caggagttct caagatggcc cttacttctg acatcaattg 6720

agatttcaag ggagtcgcca agatcatcct caggttcagt gattgctggt agccctcata 6780
```

FIGURE 16E

```
taactcaatg aaagctgtta tgctcatggc tatggtttat tacagcaaaa gaatagagat 6840

gaaaatctag caagggaaga gttgcatggg gcaaagacaa ggagagctcc aagtgcagag 6900

attcctgttg ttttctccca gtggtgtcat ggaaagcagt atcttctcca tacaatgatg 6960

tgtgataata ttcagtgtat tgccaatcag ggaactcaac tgagccttga ttatattgga 7020

gcttggttgc acagacatgt cgaccacctt catggctgaa ctttagtact tagcccctcc 7080

agacgtctac agctgatagg ctgtaaccca acattgtcac cataaatcac attgttagac 7140

tatccagtgt ggcccaagct cccgtgtaaa cacaggcact ctaaacaggc aggatatttc 7200

aaaagcttag agatgacctc ccaggagctg aatgcaaaga cctggcctct ttgggcaagg 7260

agaatccttt accgcacact ctccttcaca gggttattgt gaggatcaaa tgtggtcatg 7320

tgtgtgagac accagcacat gtctggctgt ggagagtgac ttctatgtgt gctaacattg 7380

ctgagtgcta agaaagtatt aggcatggct ttcagcactc acagatgctc atctaatcct 7440

cacaacatgg ctacagggtg ggcactacta gcctcatttg acagaggaaa ggactgtgga 7500

taagaagggg gtgaccaata ggtcagagtc attctggatg caaggggctc cagaggacca 7560

tgattagaca ttgtctgcag agaaattatg ctggatgtc tctgccccgg aaaggggggat 7620

gcactttcct tgacccccta tctcagatct tgactttgag gttatctcag acttcctcta 7680

tgataccagg agcccatcat aatctctctg tgtcctctcc ccttcctcag tcttactgcc 7740

cactcttccc agctccatct ccagctggcc aggtgtagcc acagtaccta actctttgca 7800

gagaactata aatgtgtatc ctacagggga gaaaaaaaaa aagaactctg aaagagctga 7860

cattttaccg acttgcaaac acataagcta acctgccagt tttgtgctgg tagaactcat 7920

gagactcctg ggtcagaggc aaaagatttt attacccaca gctaaggagg cagcatgaac 7980

tttgtgttca catttgttca ctttgccccc caattcatat gggatgatca gagcagttca 8040

ggtggatgga cacaggggtt tgtggcaaag gtgagcaacc taggcttaga aatcctcaat 8100

cttataagaa ggtactagca aacttgtcca gtctttgtat ctgacggaga tattatcttt 8160

ataattgggt tgaaagcaga cctactctgg aggaacatat tgtatttatt gtcctgaaca 8220

gtaaacaaat ctgctgtaaa atagacgtta actttattat ctaaggcagt aagcaaacct 8280

agatctgaag gcgataccat cttgcaaggc tatctgctgt acaaatatgc ttgaaaagat 8340

ggtccagaaa agaaaacggt attattgcct ttgctcagaa gacacacaga aacataagag 8400

aaccatggaa aattgtctcc caacactgtt cacccagagc cttccactct tgtctgcagg 8460

acagtcttaa catcccatca ttagtgtgtc taccacatct ggcttcaccg tgcctaacca 8520
```

FIGURE 16F

```
agatttctag gtccagttcc ccaccatgtt tggcagtgcc ccactgccaa ccccagaata 8580

agggagtgct cagaattccg aggggacatg ggtgggggatc agaacttctg ggcttgagtg 8640

cagaggggggc ccatactcct tggttccgaa ggaggaagag gctggaggtg aatgtccttg 8700

gaggggagga atgtgggttc tgaactctta aatccccaag ggaggagact ggtaaggtcc 8760

cagcttccga ggtactgacg tgggaatggc ctgagaggtc taagaatccc gtatcctcgg 8820

gaaggagggg ctgaaattgt gaggggttga gttgcagggg tttgttagct tgagactcct 8880

tggtgggtcc ctgggaagca aggactggaa ccattggctc cagggtttgg tgtgaaggta 8940

atgggatctc ctgattctca aagggtcaga ggactgagag ttgcccatgc tttgatcttt 9000

ccatctactc cttactccac ttgagggtaa tcacctactc ttctagttcc acaagagtgc 9060

gcctgcgcga gtataatctg cacatgtgcc atgtcccgag gcctggggca tcatccactc 9120

atcattcagc atctgcgcta tgcgggcgag gccggcgcca tgacgtcatg tagctgcgac 9180

tatccctgca gcgcgcctct cccgtcacgt cccaaccatg gagctgtgga cgtgcgtccc 9240

ctggtggatg tggcctgcgt ggtgccaggc cggggcctgg tgtccgataa agatcctaga 9300

accacaggaa accaggactg aaaggtgcta gagaatggcc atatgtcgct gtccatgaaa 9360

tctcaaggac ttctgggtgg agggcacagg agcctgaact tacgggtttg ccccagtcca 9420

ctgtcctccc aagtgagtct cccagatacg aggcactgtg ccagcatcag cttcatctgt 9480

accacatctt gtaacaggga ctacccagga ccctgatgaa caccatggtg tgtgcaggaa 9540

gagggggtga aggcatggac tcctgtgtgg tcagagccca gagggggcca tgacgggtgg 9600

ggaggaggct gtggactggc tcgagaagtg ggatgtggtt gtgtttgatt cctttggcc 9660

agataaagtg ctggatatag cattgaaaac ggagtatgaa gaccagttag aatggagggt 9720

caggttggag ttgagttaca gatggggtaa aattctgctt cggatgagtt ggggattgg 9780

caatctaaag gtggtttggg atggcatggc tttgggatgg aaataggttt gtttttatgt 9840

tggctgggaa gggtgtgggg attgaattgg ggatgaagta ggtttagttt tggagataga 9900

atacatggag ctggctattg catgcgagga tgtgcattag tttggtttga tctttaaata 9960

aaggaggcta ttagggttgt cttgaattag attaagttgt gttgggttga tgggttgggc 10020

ttgtgggtga tgtggttgga ttgggctgtg ttaaattggt ttgggtcagg ttttggttga 10080

ggttatcatg gggatgagga tatgcttggg acatggattc aggtggttct cattcaagct 10140

gaggcaaatt tcctttcaga cggtcattcc agggaacgag tggttgtgtg ggggaaatca 10200
```

FIGURE 16G

```
ggccactggc tgtgaatatc cctctatcct ggtcttgaat tgtgattatc tatgtccatt 10260

ctgtctcctt cactgtactt ggaattgatc tggtcattca gctggaaatg ggggaagatt 10320

ttgtcaaatt cttgagacac agctgggtct ggatcagcgt aagccttcct tctggtttta 10380

ttgaacagat gaaatcacat ttttttttc aaaatcacag aaatcttata gagttaacag 10440

tggactctta taataagagt taacaccagg actcttattc ttgattcttt tctgagacac 10500

caaaatgaga tttctcaatg ccaccctaat tcttttttt ttttttttt ttttgagac 10560

acagtctggg tcttttgctc tgtcactcag gctggagcgc agtggtgtga tcatagctca 10620

ctgaaccctt gacctcctgg acttaaggga tcctcctgct tcagcctcct gagtagatgg 10680

ggctacaggt gcttgccacc acacctggct aattaaattt tttttttt tttgtagaga 10740

aagggtctca ctttgttgcc ctggctgatc ttgaacttct gacttcaagt gattcttcag 10800

ccttggactc ccaaagcact gggattgctg gcatgagcca ctcaccgtgc ctggcttgca 10860

gcttaatctt ggagtgtata aacctggctc ctgatagcta gacatttcag tgagaaggag 10920

gcattggatt ttgcatgagg acaattctga cctaggaggg caggtcaaca ggaatccccg 10980

ctgtacctgt acgttgtaca ggcatggaga atgaggagtg aggaggccgt accggaaccc 11040

catattgttt agtggacatt ggattttgaa ataataggga acttggtctg ggagagtcat 11100

atttctggat tggacaatat gtggtatcac aaggttttat gatgagggag aaatgtatgt 11160

ggggaaccat tttctgagtg tggaagtgca agaatcagag agtagctgaa tgccaacgct 11220

tctatttcag gaacatggta agttggaggt ccagctctcg ggctcagacg ggtataggga 11280

ccaggaagtc tcacaatccg atcattctga tatttcaggg catattaggt ttggggtgca 11340

aaggaagtac ttgggactta ggcacatgag actttgtatt gaaaatcaat gattggggct 11400

ggccgtggtg ctcacgcctg taatctcatc actttgggag accgaagtgg gaggatggct 11460

tgatctcaag agttggacac cagcctaggc aacatggcca gaccctctct ctacaaaaaa 11520

attaaaaatt agctggatgt ggtggtgcat gcttgtggtc tcagctatcc tggaggctga 11580

gacaggagaa tcggttgagt ctgggagttc aaggctacag ggagctgcga tcacgccgct 11640

gcactccagc ctgggaaaca gagtgagact gtctcagaat ttttttaaaa aagaatcagt 11700

gatcatccca acccctgttg ctgttcatcc tgagcctgcc ttctctggct ttgttcccta 11760

gatcacatct ccatgatcca taggccctgc ccaatctgac ctcacaccgt gggaatgcct 11820

ccagactgat ctagtatgtg tggaacagca agtgctggct ctccctcccc ttccacagct 11880

ctgggtgtgg gaggggttg tccagcctcc agcagcatgg ggagggcctt ggtcagcatc 11940
```

FIGURE 16H

```
taggtgccaa cagggcaagg gcggggtcct ggagaatgaa ggctttatag ggctcctcag 12000

ggaggccccc cagccccaaa ctgcaccacc tggccgtgga caccggt          12047
```

FIGURE 17

```
cgagcggccc ctcagcttcg gcgcccagcc ccgcaaggct cccggtgacc actagagggc 60

gggaggagct cctggccagt ggtggagagt ggcaaggaag gaccctaggg ttcatcggag 120

cccaggttta ctcccttaag tggaaatttc ttcccccact cctccttggc tttctccaag 180

gagggaaccc aggctgctgg aaagtccggc tggggcgggg actgtgggtt caggggagaa 240

cggggtgtgg aacgggacag ggagcggtta gaagggtggg gctattccgg gaagtggtgg 300

ggggagggag cccaaaacta gcacctagtc cactcattat ccagccctct tatttctcgg 360

ccgctctgct tcagtggacc cggggagggc ggggaagtgg agtgggagac ctaggggtgg 420

gcttcccgac cttgctgtac aggacctcga cctagctggc tttgttcccc atccccacgt 480

tagttgttgc cctgaggcta aaactagagc ccaggggccc caagttccag actgcccctc 540

ccccctcccc cggagccagg gagtggttgg tgaaaggggg aggccagctg gagaacaaac 600

gggtagtcag ggggttgagc gattagagcc cttgtaccct acccaggaat ggttggggag 660

gaggaggaag aggtaggagg taggggaggg ggcggggttt tgtcacctgt cacctgctcg 720

ctgtgcctag ggcgggcggg cggggagtgg ggggaccggt ataaagcggt aggcgcctgt 780

gcccgctcca cctctcaagc agccagcgcc tgcctgaatc tgttctgccc cctccccacc 840

catttcacca ccaccatg                                            858
```

FIGURE 18

```
aagcttccac aagtgcattt agcctctcca gtattgctga tgaatccaca gttcaggttc 60

aatggcgttc aaaacttgat caaaaatgac cagactttat attcttacac caacatctat 120

ctgattggag gaatggataa tagtcatcat gtttaaacat ctaccattcc agttaagaaa 180

atatgatagc atcttgttct tagtcttttt cttaataggg acataaagcc cacaaataaa 240

aatatgcctg aagaatggga caggcattgg gcattgtcca tgcctagtaa agtactccaa 300

gaacctattt gtatactaga tgacacaatg tcaatgtctg tgtacaactg ccaactggga 360

tgcaagacac tgcccatgcc aatcatcctg aaaagcagct ataaaaagca ggaagctact 420

ctgcaccttg tcagtgaggt ccagatacct acag                             454
```

```
g atg acc ggc tca acc atc gcg ccc aca acg gac tat cgc aac acc act 49
  Met Thr Gly Ser Thr Ile Ala Pro Thr Thr Asp Tyr Arg Asn Thr Thr
   1               5                   10                    15

gct acc gga cta aca tct gcc cta aat tta ccc caa gtt cat gcc ttt    97
Ala Thr Gly Leu Thr Ser Ala Leu Asn Leu Pro Gln Val His Ala Phe
            20                  25                  30

gtc aat gac tgg gcg agc ttg gac atg tgg tgg ttt tcc ata gcg ctt   145
Val Asn Asp Trp Ala Ser Leu Asp Met Trp Trp Phe Ser Ile Ala Leu
        35                      40                  45

atg ttt gtt tgc ctt att att atg tgg ctt att tgt tgc cta aag cgc   193
Met Phe Val Cys Leu Ile Ile Met Trp Leu Ile Cys Cys Leu Lys Arg
        50                  55                  60

aga cgc gcc aga ccc ccc atc tat agg cct atc att gtg ctc aac cca   241
Arg Arg Ala Arg Pro Pro Ile Tyr Arg Pro Ile Ile Val Leu Asn Pro
65                  70                  75
                                                            80

cac aat gaa aaa att cat aga ttg gac ggt ctg aaa cca tgt tct ctt   289
His Asn Glu Lys Ile His Arg Leu Asp Gly Leu Lys Pro Cys Ser Leu
                85                  90                  95

ctt tta cag tat gat taa
Leu Leu Gln Tyr Asp                                               307
                100
```

FIGURE 19